THE American Journal OF Gastroenterology

VOL. 30, NO. 4 OCTOBER, 1958

Official Publication
AMERICAN COLLEGE
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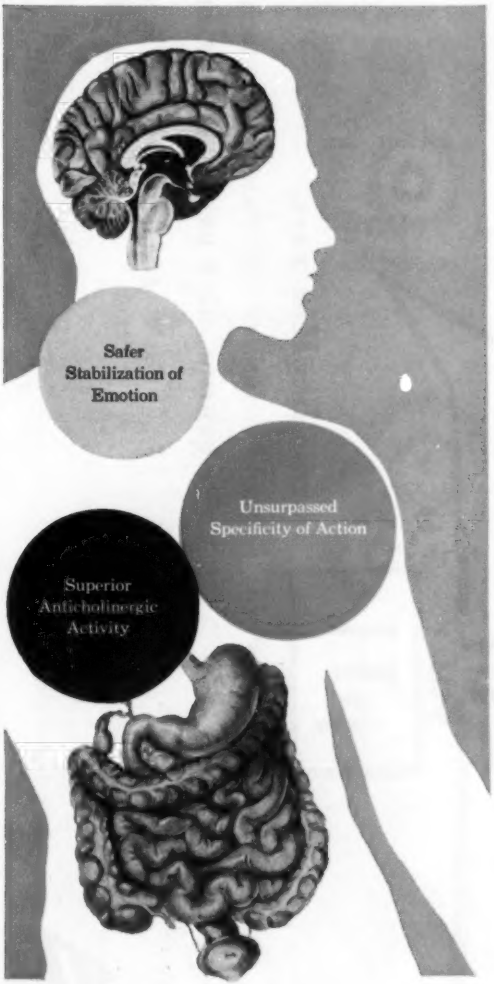

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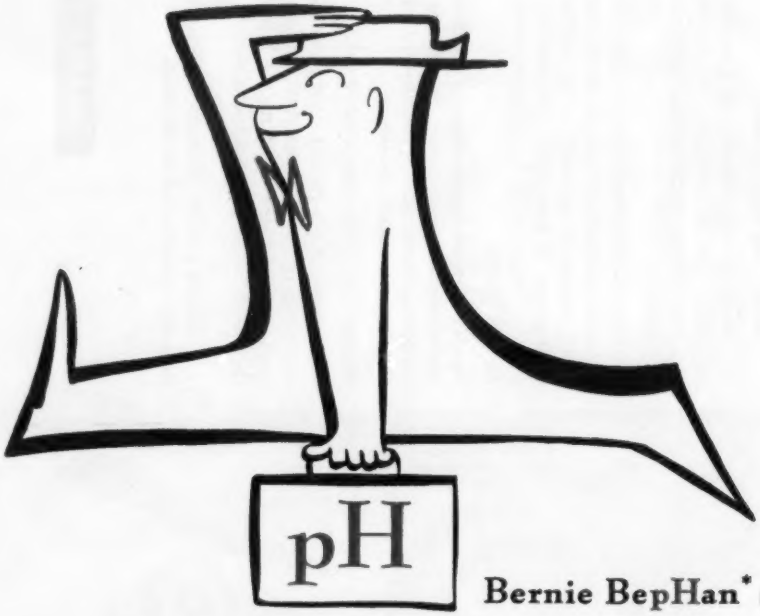

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THE American Journal OF Gastroenterology

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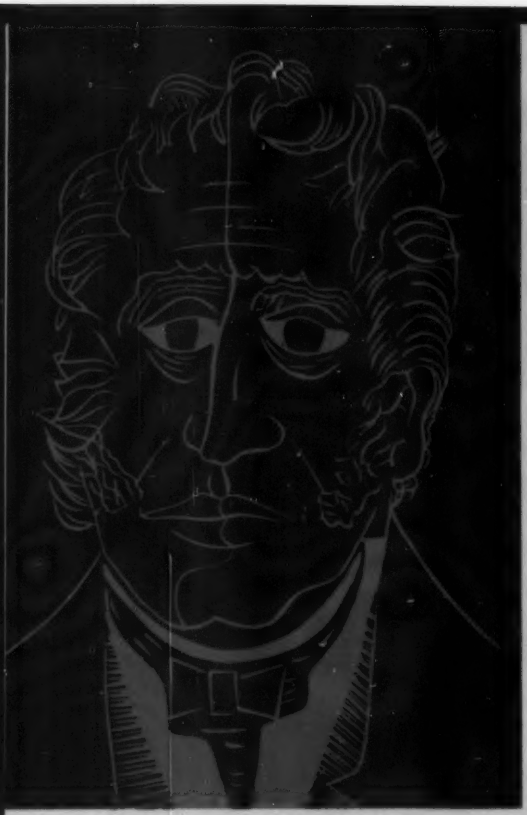

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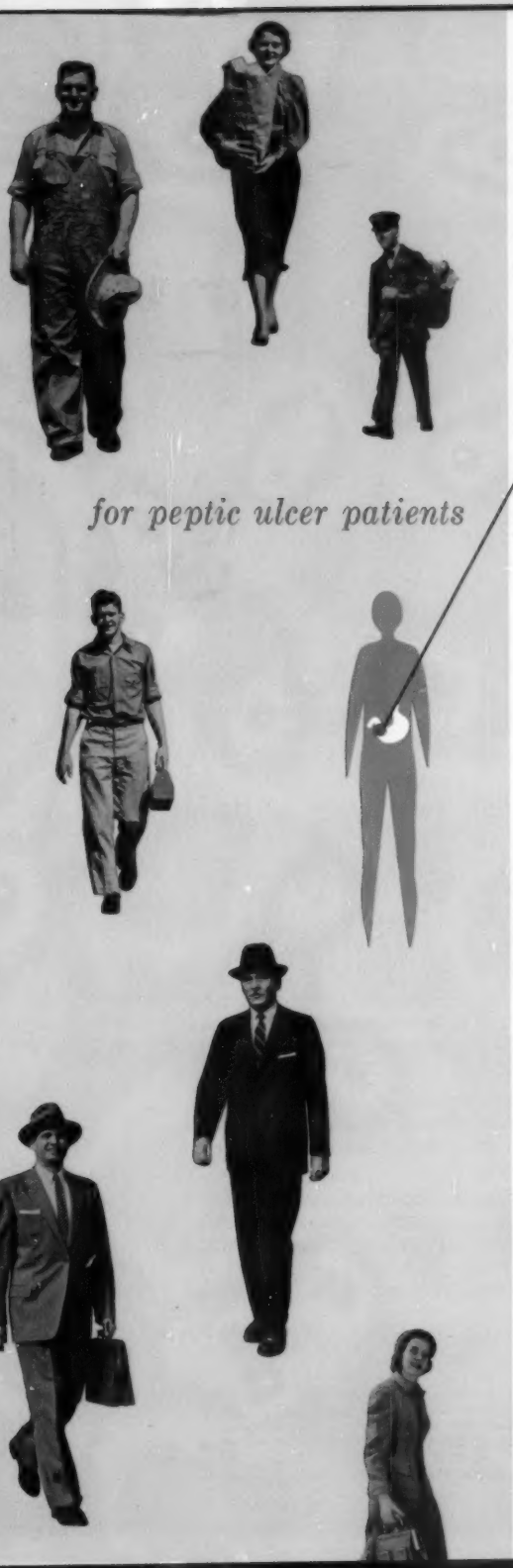

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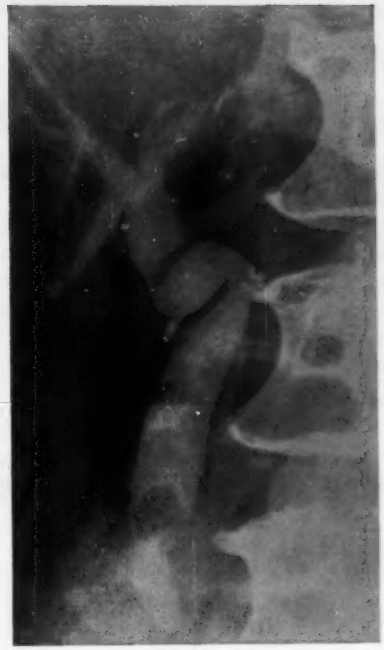

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THE American Journal OF Gastroenterology

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VOLUME 30 OCTOBER, 1958 NUMBER 4

CLINICOPATHOLOGIC CORRELATIONS IN FATTY NUTRITIONAL CIRRHOSIS*

STANLEY L. ROBBINS, M.D.†

Boston, Mass.

In the course of pathologic study of cases of fatty nutritional cirrhosis certain interesting and changing aspects have been noted which I should like to present. At the outset let me clarify some of the present terminology relating to this condition.

The term, fatty nutritional cirrhosis, is the current, most-favored designation for the form of liver disease formerly referred to as Laennec's cirrhosis or alcoholic cirrhosis. The name itself, i.e. fatty nutritional cirrhosis is useful because it clearly points out, perhaps the two most well-founded observations bearing on this form of liver disease. In the early stages the liver is invariably fatty, and present evidence strongly suggests that this fatty change is important in the genesis of the later developing diffuse fibrosis. And secondly, according to our present evidence, the etiology of this condition involves some nutritional deficiency. I do not intend to enter further into the controversy that surrounds the genesis of this liver disease, nor to get involved in the role of alcoholism in its production. Suffice it to say that chronic alcoholism is abundantly present in the great majority of cases of fatty nutritional cirrhosis that we encounter. To my knowledge, it has not yet been established whether this alcoholic consumption acts in a direct injurious fashion as a potentiating agent for some other hepatotoxin, or as a caloric or nutritional substitute for more adequate types of food. Seife, Kessler and Lisa[1] have shown that if you routinely biopsy the enlarged livers of patients who have a considerable consumption of alcohol, fatty changes suggestive of the early stages of nutritional cirrhosis are found in about 70 per cent of the cases.

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*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Boston, Mass., 24, 25, 26 October 1957.

†Associate Director, Mallory Institute of Pathology; Professor of Pathology, Department of Pathology, Boston University School of Medicine.

Turning now to some of the evolutionary changes that we believe are occurring, let us consider first the incidence of fatty nutritional cirrhosis. The figures which I am about to present are derived from the autopsy population of the Mallory Institute of Pathology of the Boston City Hospital. This is, as you may know, a large municipal hospital serving principally a middle to lower economic group of people, among whom chronic alcoholism is an all too prevalent problem. Between the years 1897 to 1932 there was an incidence of .13 per cent of all forms of cirrhosis of the liver in over 9,000 autopsies. If we compare this incidence with 1952, the frequency of cirrhosis in the autopsy population rose to 14 per cent. In 1953 it was 16 per cent. In 1954, 19 per cent. In 1955, approximately 20 per cent. While these data refer to all types of cirrhosis, in our present autopsy population at least 60 to 70 per cent of all types of cirrhoses are of the fatty nutritional type. It is then safe to say that we are witnessing a progressive increase in the incidence of this type of disease and that approximately one in ten of the patients who come to autopsy at this Institute suffers from fatty nutritional cirrhosis. I have no ready explanation for this progressive rise in incidence. Some of it may reflect the fact that other outlets of the stream of mortality are narrowed or shut off, and liver disease becomes one of the more important outflows. This could not account, however, for the striking increased frequency we have cited. Alternately, it is possible that in former years, when our understanding of liver physiology was more imperfect, many of these patients might have died in the stages of fatty liver, perhaps from liver insufficiency or some intercurrent disease; whereas now improved understanding and therapy permit these people to survive with their fatty livers and thus to develop at a later date, nutritional cirrhosis. Lastly, as a final speculation, the increased usage of alcohol and the rise of chronic alcoholism as a sociomedical problem may simply parallel the mounting problem of juvenile delinquency and all the other expressions of the weakened morality of our "Age of Anxiety".

Let us now turn to a somewhat different area of this subject, namely the correlation of the morphologic disease with the clinical signs and symptoms. To this point, I have referred to fatty nutritional cirrhosis as though it were a single, homogenous entity. The fact is that within the term, fatty nutritional cirrhosis, there are several different clinical and anatomic patterns. Before we can attempt to correlate the clinical changes, we should first establish the various anatomic stages that can be identified. There are, it seems to us, three distinctive stages of Laennec's cirrhosis. 1. The fatty, nonfibrotic stage, at which time the diagnosis may be difficult to establish clinically. 2. Fibrofatty stage of the well-developed nutritional cirrhosis, at which time the liver is usually enlarged but at the same time is tough and fibrotic. 3. The advanced fibrous stage at which time the liver becomes small and atrophic. Each of these stages has distinct and somewhat different clinical significances. In the fatty stage, the liver is enlarged, sometimes massively, up to as much as 6 kilos. It is readily palpable, soft, often has a blunted, rounded anterior edge and is sometimes

tender. During this stage there are often very few clinical complaints. Ascites and edema are not frequent. Jaundice may be present, but is usually mild and often is absent. The patient is usually not wasted. There are often disturbances in the battery of liver function studies, but these are not extreme. During this stage there is little evidence of portal hypertension in the form of splenomegaly or varices, although these very infrequently do develop. One of three pathways may ensue from this point. Most favorably, the patient goes on a more adequate diet, and the fat, as you know, is completely mobilizable. The liver may, therefore, revert to normality since there is little or no fibrosis. We have been able, by serial biopsy studies, to demonstrate quite remarkable rapid mobilization of fat and progressive diminution of liver size in as short a time as several weeks. There has been, along with these changes, progressive improvement in the liver function studies. The second pathway that these fatty livers may follow is the slow development of diffuse fibrosis, leading to the classic, full-blown stage of fatty nutritional cirrhosis. Usually, this is the pathway seen in patients who maintain deficient diets. The third possible pathway that may be followed, and one that is perhaps not as widely appreciated, is the sudden development of a solitary massive wave of necrosis or multiple, less severe recurrent waves of necrosis, both leading to hepatic insufficiency. Thus it is possible for a patient in the early fatty stages of nutritional cirrhosis to go suddenly into hepatic failure and coma without ever developing frank, diffuse, fibrous scarring or signs of portal hypertension. The exact genesis of these episodes of acute necrosis are poorly understood. Sudden increased metabolic demand upon the liver may lead to excess stress and consequent degeneration and death of liver cells. Alternately, worsening of the deficiency state may lead to these acute necroses. In this respect, there is abundant evidence from animal experimentation that dietary deficiencies, particularly of the sulphur-bearing amino acids, may result in necrosis of liver cells. Another work suggests that selenium deficiency may cause acute hepatic necrosis. It is entirely possible then that the nutritional deficiencies that lead to fatty cirrhosis may, at the same time, be accompanied by other deficiencies that lead to acute necrosis.

The second clinically significant pattern of fatty nutritional cirrhosis is the classic fibrofatty stage already mentioned. The liver is now diffusely fibrotic, scarred, has the classic hobnail appearance, and is usually slightly enlarged, but may be normal in size. It is often palpable and sometimes imparts the impression of some irregularity of the anterior liver edge on palpation, but frequently the discrete nodules are not detectable. Splenomegaly is common. *Spider nevi*, palmar erythema, ascites, peripheral edema, weight loss, deranged liver function studies and all the classic manifestations of diffuse liver disease are now present. It must not be forgotten, however, that at this stage of the cirrhosis the patient may be entirely free of symptoms and have only laboratory evidence of deranged function—the so-called stage of compensated liver disease. What are the possible pathways followed by this fibrofatty liver? 1. The patient

may remain in a stage of compensated liver disease for the remainder of his natural life and die of some completely unrelated, intercurrent entity. It must be admitted, however, that these patients are particularly prone to infections and a considerable number die of bacterial and viral infections, predisposed to or aggravated by the underlying, diffuse liver disease. 2. These patients may have progressive fibrosis and scarring of their livers until they reach the stage of marked, fibrous atrophy, at which time the threshold of hepatic reserve is passed, and death occurs due to liver insufficiency. 3. Some acute, intercurrent stress may cause a relative hepatic insufficiency. This is the basis for sudden liver failure in the course of a severe bacterial pneumonia, postoperatively, following sudden blood loss as from rupture of esophageal varix, or following an episode of shock due to any one of a number of possible causes. Whatever the precipitating factor, these marginally compensated livers cannot maintain normal metabolic function in the presence of some increased work load or further debilitating condition. 4. A fourth pathway that may be followed is a sudden development of a wave of acute necrosis with the rapid progression into hepatic insufficiency and failure. 5. An additional pathway is death due to one of the complications of cirrhosis of the liver. In the series reported by Ratnoff and Patek[2,3] they state that hematemesis is a cause of death in up to 26 per cent of their patients. A very small percentage of patients with fatty nutritional cirrhosis develop a primary carcinoma of the liver, and it is of interest that the frequency of carcinoma, complicating fatty nutritional cirrhosis seems to be on the increase, rising from an averge frequency of one per cent in the 1920's to a figure of approximately three per cent in the 1940's.

The third stage of the disease to which I have made previous references, is the so-called fibroatrophic stage also known as the burnt-out end stage of nutritional cirrhosis. The liver is now shrunken to smaller than normal size, has a deeper brown coloration than the earlier stages due to the almost total disappearance of fat, the lobulation is somewhat more irregular and nodular, and in many instances there are large, broad, fibrous scars, suggesting that large areas of the liver substance have undergone total necrosis. The magnitude of these scars is perfectly compatible with what has always been referred to as healed, acute yellow atrophy or postnecrotic scarring. In fact, there is, indeed, some question as to whether these large scars are not due to massive necrosis of dietary origin, simulating the experimental massive necrosis caused by diets deficient in methionine and cystine. Not infrequently, it is quite impossible to differentiate the late burnt-out stage of a fatty nutritional cirrhosis from a postnecrotic scarring, so we must entertain the possibility that in these severely damaged livers, extreme scarring tends to cause a similarity between the various patterns of cirrhosis. These markedly atrophic livers obviously have a narrow hepatic reserve and may follow any of the pathways described for the second fibrofatty stage. Hepatic insufficiency and complications related to portal hypertension, however, are significantly more common at this stage. There is abundant

evidence that in these shrunken fibrotic livers there are many anastomoses between the portal vein and the hepatic artery and between portal vein and hepatic vein. These anastomoses shunt blood from the arterial circulation into the portal circulation, thus raising the pressure in the portal area of drainage. At the same time, these anastomoses between portal vein and hepatic vein tend to cause blood to bypass the hepatic substance and thus further reduce the functional efficiency of the liver. These are the patients who have persistent and tractable ascites that rapidly re-accumulate. Varices are prominent problems with their bleeding episodes, and these are the patients that have multiple episodes of hepatic insufficiency, usually precipitated by intercurrent stress, terminating in a final, irreversible hepatic failure.

In summary then, there appear to be three stages of fatty nutritional cirrhosis having distinctive morphologic patterns and distinctive clinical symptom complexes. The early fatty stage, while usually causing few subjective symptoms, is nonetheless of great significance on two scores—one, it may be interrupted at any point by a wave of acute necrosis leading to sudden liver insufficiency; and two, it is the forerunner, unless the progress of the disease is halted, of further fibrous irreversible scarring.

The fibrofatty stage is the commonly recognized classic stage of cirrhosis, having many manifestations relating to liver insufficiency and portal hypertension.

In the third, most advanced, fibroatrophic stage, portal hypertension becomes the dominant problem. But hepatic function may also become manifestly insufficient when any sudden stress is thrown upon these already damaged livers.

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Discussion

Dr. H. Edward MacMahon (Boston, Mass.):—This is a most unexpected opportunity to tell Dr. Robbins how very much I have enjoyed his paper, for I did not know until now that I was to be invited to participate in this discussion.

There are several points that I think should be stressed in this paper. First there is the changing pattern of the disease which is so dependent on the element of time. The second is concerned with the need for more diagnostic biopsies in studying the biography of a single case. Much of our thinking today is based on studies of large series of cases in which it is assumed, in the case of alcoholic cirrhosis, that each of these has run a fairly standard course. We recognize what we consider to be the early stages histologically, just as we recognize what we believe to be the end stages of the same disease. Probably

much of this is based on fact, but in the end stages of cirrhosis, patterns become much less specific and several diseases that may have had an entirely different beginning may terminate in a similar fashion. Third, one should not be afraid, in diagnosing liver biopsies or even in classifying cirrhosis, when seen at the autopsy table, to admit that one is not certain of the exact pathogenesis of the lesion under consideration. Some patterns are so typical, while others are so difficult to classify. Fourth, since one is dealing with an organ that is so susceptible to a number of different diseases, the possibility of combination forms of cirrhosis must always be kept in mind, since one type of cirrhosis appears to offer little or no protection against another. A fifth point that I would like to mention is that our histological classification of liver disease, particularly the cirrhoses, is still the best that we have, and the most reliable in terms of interpreting disturbances in function, which manifest themselves in clinical signs and symptoms. To express this in another way, one might say that any attempt to treat a patient with liver disease without an understanding of the pattern of pathology that is causing the signs and symptoms could only lead to confusion. Lastly, and I believe this is no secret, the clinician who will take the trouble to discuss his case with his own pathologist, will get a much better opinion from a needle biopsy than were he to send in the biopsy alone with no personal contact from the pathologist. The pathologist, of course, will base his diagnosis entirely on what he sees in his section, but he will look a little harder and he will see a little more, if he is allowed to participate in the responsibility and care of the patient.

Clinicopathological Conference*

from the New England Deaconess Hospital, Boston, Mass.

Dr. McKittrick:—Just so we will all become oriented, I am Dr. Leland S. McKittrick†. Immediately to my right is Dr. William A. Meissner‡, of Boston. The other men I know I need not introduce to you, but just so there can't be any misunderstanding, Dr. Owen H. Wangensteen** is sitting there in the middle, and Dr. I. Snapper†† is on the end.

I think there have been passed around to you these two cases. They are both, I suspect, extremely simple and very obvious to all in the audience, as I am sure they are to the gentlemen at the table here, and I imagine that the most productive way to do this is to have each one, Dr. Snapper and then Dr. Wangensteen, discuss each his own case. I would hope that at the end of each presentation the audience will feel very free to make some suggestions, which I know will be appreciated. You might even ask any questions that you might care to.

Dr. Meissner, you probably have both of the records here, and if there is anything that is not available to either of you gentlemen and we can supply it, we will be glad to do that.

Dr. Wangensteen, I happen to have in my pocket a letter that I received from the first surgeon that operated on your patient, which I will read to you and to the audience generally, simply because it seems to me you should be privileged to have that information, and now, without any further ado, Dr. Snapper, wouldn't you like to take over?

Protocol—I

A 64-year old salesman was admitted with the chief complaints of extreme fatigue and a weight loss of 35 pounds during the preceding two years. He had no anorexia, but was afraid to eat because of discomfort from fullness in the abdomen after meals. About a month prior to admission his bowels, previously constipated, became loose; his stools were grayish-yellow and occasionally looked like fat, but no blood was noted. Bowel movements relieved the abdominal discomfort. Two to three months prior to admission he noted polyuria and nocturia. There was a chronic, nonproductive cough.

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*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Boston, Mass., 24, 25, 26 October 1957.

†Clinical Professor of Surgery, Harvard Medical School; Consulting and Visiting Surgeon, Massachusetts General Hospital, Boston, Mass.

‡Pathologist, New England Deaconess Hospital, Boston, Mass.

**Professor and Chairman, Department of Surgery, University of Minnesota School of Medicine, Minneapolis, Minn.

††Director of Medical Education, Beth-El Hospital, Brooklyn, N. Y.

Family history:—A sister had diabetes mellitus, two brothers and daughter had died of cancer.

Past history:—He had for many years been a moderate drinker but had not used alcohol for three or four years prior to admission. Eight months before admission he had been hospitalized for repair of a ventral hernia with an uneventful postoperative course. At that time he had no abdominal complaints except for chronic constipation, and x-ray studies of the chest, upper gastrointestinal tract and colon were normal. Laboratory studies were likewise normal at that time, except for an elevated sedimentation rate and a white blood cell count varying between 20,000 and 25,000 with a normal differential.

Physical examination on the last admission showed an alert, emaciated patient. Skin rather dark, without local areas of increased pigmentation. Weight 105 pounds. Blood pressure 105/80. Temperature 98.6. Pulse rate 90. Respiration rate 20. Tongue normal. Heart and lungs normal except for a few scattered rales in both lung bases. Abdomen seemed somewhat distended and doughy. Liver was not felt. Rectal examination negative. Slight ankle edema. Several small inguinal nodes were palpable, nontender and discrete.

Roentgenograms of the chest revealed no abnormalities. Gastrointestinal films showed hypomotility and a very coarse pattern in all segments of the small bowel. There was a smooth filling defect of the greater curvature.

Peritoneoscopy revealed normal liver. No free fluid and no abnormalities of the intestinal surfaces. Needle biopsy showed normal liver.

Course in hospital:—At time of admission and subsequently, patient passed yellow-gray, foul-smelling stools, that on microscopic examination showed occasional fat crystals and globules. During the hospital course, the patient received crude liver extract, Vitamin B-complex, Vitamin B_{12}, lipotropic substances, and Vitamin C. Testosterone, protein hydrolysate solutions, human albumin, blood transfusions, intravenous fat emulsions, folic acid, and cortisone were all administered for varying intervals. No treatment, however, seemed to influence the slow and steady downhill course of the patient. The diarrhea continued, and during the last two weeks of his life became very severe. Afebrile during entire hospital course. Gradually became more confused and drowsy. Rales developed in both lungs and he died on the 64th hospital day.

REPRESENTATIVE LABORATORY FINDINGS, LAST ADMISSION

Hemoglobin, gm./100 c.c.	9.5
Red blood cells, millions/cu. mm.	3.39
White blood cells, thousands/cu. mm.	11.7
Differential white cell count	Normal
Platelet count	Normal
Sedimentation rate (Wintrobe)	Normal

Routine urinalysis	Normal
Fasting blood sugar, mg./100 c.c.	100
Blood urea nitrogen, mg./100 c.c.	14
Serum protein, gm./100 c.c.	3.6
Serum albumin	2.1
Serum globulin	1.5
Albumin/globulin ratio	1.4
Serum calcium, mg./100 c.c.	7.8
Serum phosphorus, mg./100 c.c.	2.9
Serum bilirubin, mg./100 c.c.	0.30
Thymol turbidity test	Normal
Thymol flocculation test	Normal
Sulfobromphthalein retention	Normal
Alkaline phosphatase, Bodansky units	2.1
Hinton test	Negative
Basal metabolic rate	Plus 29%
Radioactive iodine uptake	Normal
Oral glucose tolerance curve	Decreased
Percentage fecal fat in 72-hour dried specimen	56-60
Gastric aspiration, free HCl	Present
Duodenal aspiration, viscosity	Normal
Duodenal aspiration, amylase	Normal
Duodenal aspiration, trypsin	Normal
Duodenal aspiration, lipase	Normal
Duodenal aspiration, phosphatase	Normal

Dr. I. Snapper:—This 64-year old salesman was admitted with the chief complaints of loss of weight and fatigue. Every disease starts with fatigue, whether it is flat feet or a tumor of the brain, or any other ailment, located between the feet and the brain. Therefore, fatigue does not necessarily indicate the presence of a serious disease. Weight loss of 35 pounds during the preceding two years, however, gives rise to great concern. Yet there was no anorexia, although he was afraid to eat because of discomfort from fullness in the abdomen after meals.

One month previous to admission, his bowels, previously constipated, became loose. His stools were grayish-yellow and occasionally looked like fat. No blood was noted and thus there was no ulceration, distal to the splenic flexure. Bowel movements relieved the abdominal discomfort. Two or three months prior to admission he noted polyuria and nocturia. There was a chronic, nonproductive cough.

A sister had diabetes mellitus and two brothers and a daughter had died of cancer. He had for many years been a moderate drinker, but had not used alcohol for three or four years prior to admission. Eight months before admission he had been hospitalized for repair of a ventral hernia with an uneventful postoperative course.

On admission there was an elevated sedimentation rate and a leucocytosis varying from 20,000 to 25,000. He was alert, emaciated, skin rather dark, with increasing pigmentation, and weight 105 pounds. His blood pressure was 105/80, his temperature was normal, pulse rate 90, and respiration rate 20; tongue normal, heart and lungs normal except for a few scattered rales in both lung bases. His abdomen was somewhat distended and doughy. Since he weighed only 105 pounds and had a distended abdomen, an abdominal disease is highly probable. The liver was not felt. The rectal examination was negative. There was slight ankle edema. Several small inguinal nodes were palpable, nontender, and discrete.

Roentgenograms of the chest were normal. The gastrointestinal film showed hypomotility and a very coarse pattern in all segments of the small bowel. This gives the impression of a deficiency pattern especially in the presence of fatty diarrhea. There was a *smooth* filling defect of the greater curvature.

The peritoneoscopy revealed a normal liver, no free fluid and no abnormalities of the intestinal surfaces. Needle biopsy showed a normal liver structure.

At the time of admission and subsequently, the patient passed yellow-gray, foul-smelling stools, that on microscopic examination showed occasional fat crystals and globules. The latter data I can only take under advisement, because if the stools were really foul-smelling and gray, due to the presence of fat, then the microscopic examination should have revealed much more fat globules and crystals. Modern gastroenterologists stay as far removed as possible from all the secreta of the gastrointestinal tract. Nothing is more systematically avoided than the microscopic examination of the stool,—this foul-smelling excrete from the intestine. Consequently the correct methods to discover microscopic fat in the stool have gone into oblivion. For the time being we thus have to assume that this patient had fatty stools—notwithstanding the equivocal microscopic report.

In the hospital he received crude liver extract, Vitamin B-complex, Vitamin B_{12}, lipotropic substances, and Vitamin C. Testosterone, protein hydrolysate solutions, human albumin, blood transfusions, intravenous fat emulsions, folic acid, and cortisone were all administered for varying intervals—in other words he received the last rites of modern therapy. No treatment, however, seemed to influence the slow and steady downhill course of the patient. The diarrhea continued and during the last two weeks of his life became very severe. He was afebrile during the entire hospital course, and gradually became more confused and drowsy. Rales developed in both lungs and he died on the 64th hospital day.

This then was on old gentleman who regularly lost weight, had a distended abdomen, developed diarrhea until he died, and we have to ask ourselves what could this man have suffered from. Could it have been sprue, in this case nontropical sprue? This is a question of semantics. What is the meaning of the designation sprue?

Sprue, since olden times, was a disease where fatty diarrhea was present and where at autopsy no cause for the fatty diarrhea was found. Nowadays in sprue biopsies of the villi of the small intestine, performed during life, show swelling and other changes of the villi. At the autopsy, due to postmortal changes these anomalies cannot be visualized any more. There is no reason to assume that this man, in the later years of his life, developed sprue and within one year died of it. Personally I think it highly probable that in this patient at autopsy an anatomical reason for the fatty diarrhea was present.

Older people often develop carcinoma of the pancreas and the carcinoma of the pancreas obstructs the pancreatic duct. Then no pancreatic juice, i.e. no lipase, can reach the intestine and the neutral fats are not hydrolized to fatty acids. The human intestine cannot absorb neutral fats; it can only absorb fatty acids. Therefore, in the absence of pancreatic juice only neutral fats are present in the intestine, and since neutral fats are not absorbed, fatty diarrhea must result.

Whereas fatty acids conjugate with calcium to form calcium soaps, neutral fats do not bind calcium. Thus fatty diarrhea due to the absence of pancreatic juice does not give rise to hypocalcemia. In this patient there is hypocalcemia and in addition the serum phosphorus is low. We, therefore, are justified in concluding that in his case not only neutral fats but also fatty acids were eliminated in great quantities. Finally the protocol mentions a normal amylase, trypsin, and lipase content of the duodenal juice and we, therefore, can be certain that pancreatic juice did reach the duodenum. Under the circumstances one cannot diagnose a carcinoma of the pancreas.

What other causes of fatty diarrhea must be considered in this patient? Sixty years ago when tuberculosis was rampant children died with a distended abdomen and fatty diarrhea. At autopsy tuberculosis of the mesenteric lymph nodes was often found,—a disease called *tabes mesaraica*. Then a new disease was recognized which in the U.S.A. goes under the name of celiac disease and which in other countries is named Gee-Herter's disease, as a tribute to the important contributions our compatriot Herter made in this field. At the autopsy of celiac disease, no anatomical changes were found. Therefore celiac disease was defined as infantile sprue and the concept that tuberculous lymph nodes could cause fatty diarrhea—the *tabes mesaraica*—was given up.

About 40 years ago Dr. Ryle in Cambridge, England, reinvestigated this problem and found that infiltration of mesenteric lymph nodes either by tuberculosis or, more frequently by carcinoma, and occasionally by lymphoma, may obstruct the lacteals which transport the fat from the intestine towards the thoracic duct. In such cases the fat transported from the intestine suffers and fatty diarrhea results.

In this patient we have to discuss the possibility of a carcinoma of one of the abdominal organs with infiltration of the mesenteric lymph nodes, obstruction of fat transport and fatty diarrhea.

I would therefore consider, without having seen the x-rays—

Dr. McKittrick:—Would you like to see the x-rays?

Dr. Snapper:—without having seen the x-rays, that this could be an obstruction of the mesenteric nodes by a malignancy—which opinion I may change after I have seen the x-rays.

Dr. Wangensteen:—How about a basal metabolism?

Dr. Snapper:—Nobody does a basal metabolism anymore.

Dr. Ty:—(Slide) This is a 30-minute examination. This shows the smooth antral region, and in 30 minutes the barium seems to be dispersed all around to the distal small bowel, and one can note that the valves of conniventes are widely spaced in all its segments. It is a coarsening effect.

(Slide) This is a 90-minute film, which showed the same appearance. The stomach is normal.

Dr. Snapper:—Do you still see the lesion? Can we see something of the 90-minute film?

Dr. Ty:—No, you cannot see it there again except for this filling defect in the stomach.

Dr. Snapper:—Well, beggars cannot be choosers, and we ought to be thankful for small mercies. A definite opinion about the lesion of the stomach can hardly be given on these roentgenograms, because the stomach is overfilled with barium. A study of the mucous membrane pattern would be helpful, because it would give information as to whether or not the mucous membrane was destroyed. In the latter case one would have to accept the presence of a neoplasm.

Since, then, the presence of a carcinoma is far from proven, other diseases which infiltrate the lymph nodes and give rise to fatty diarrhea must be considered as for instance Whipple's disease. This is a lipoid granuloma-like disease, present both in the lymph nodes and also in the wall of the intestine. With the PAS stain a special mucoprotein can be visualized within the lesions.

Whipple's disease, of course, in the practice of medicine, does not occur as frequently as it occurs at CPC's. One has to cope with the realities, however, and under the circumstances this disease must be seriously considered.

Dr. McKittrick:—Would the peritoneoscopy be of any significance so far as excluding carcinoma is concerned?

Dr. Snapper:—Well, sir, this is a rhetorical question. You can answer it better than I can.

Dr. McKittrick:—If I know who did it—is that what you mean?

Dr. Snapper:—In many cases with malignant infiltration of lymph nodes peritoneoscopy has revealed a normal peritoneum. Especially a small carcinoma of the stomach cannot always be seen during peritoneoscopy.

I repeat that since we have no clear cut evidence of malignancy, we have to consider a nonmalignant infiltration of the lymph nodes, as for instance is the case in Whipple's disease.

On the other hand a small carcinoma of the tail of the pancreas with secondary infiltration of the lymph nodes cannot be completely excluded.

Dr. Wangensteen:—You didn't say anything about fibrocystic disease.

Dr. Snapper:—During the childhood of this patient, the children with fibrocystic disease still died before they reached puberty. Now these children can be kept alive by antibiotics which prevents death by bronchopneumonia. The latter disease was 30 years ago the unavoidable complication of fibrocystic disease of the lung.

Dr. Wangensteen:—Does it ever come to maturity?

Dr. Meissner:—Not as full blown.

Dr. Snapper:—All this is due to the fact that cystic disease is present both in the pancreas and in the lungs.

Dr. Wangensteen:—I should like to ask the roentgenologist if the filling defect in the distal end of the stomach was persistent.

Dr. Ty:—It was persistently seen.

Dr. Wangensteen:—That should be a leiomyoma with free acid in the stomach, or leiomyosarcoma.

Dr. Snapper:—It has no cat's eye.

Dr. Wangensteen:—Is blood flow involved? With a leiomyosarcoma—

Dr. Snapper:—It has no cat's eye, which means no ulceration: this makes a leiomyosarcoma improbable. If the mucous membrane was not destroyed then it could be a leiomyoma, or a lipoma, or a neurofibroma.

Dr. Wangensteen:—That pattern of the small intestine would rule out tuberculosis of the small colon—no stricture.

Dr. Snapper:—This is a small intestine filled with fatty fermenting masses. With the fatty stool so much Vitamins D and B are lost that an avitaminosis pattern results as is present in this case.

Dr. McKittrick:—The question I was going to ask, Dr. Snapper, is this: supposing, if you were to see a stomach in which you could see the mucosal outline well, and you were satisfied that you had a mucosal outline which was within normal limits, and therefore would feel that you would not be justified in making a diagnosis of carcinoma of the stomach, which, then, would you put as your more probable diagnosis?

Dr. Snapper:—I would say that one still could not exclude a malignancy of one of the organs which cannot be visualized by x-ray especially the pancreas. I would, however, then put first the possibility that a nonmalignant infiltration of the mesenteric glands existed,—tuberculosis, perhaps Hodgkin's disease but *especially* lipoid granuloma.

Dr. McKittrick:—I was asking myself a question here which I couldn't answer, so I am going to ask it of you, and Dr. Wangensteen, and Dr. Meissner. I was just trying to think how commonly one sees this rather massive infiltration of the mesenteric nodes in carcinoma without ascites.

Dr. Snapper:—Frequently enough to diagnose at a C.P.C.

Dr. McKittrick:—You can't bet on a horse that usually wins at a CPC, can you?

Dr. Snapper:—A successful CPC discusser is to be compared with a man who always after reading the first ten pages of a detective story can indicate the culprit. Nevertheless this ingenious fellow would be a failure if he would have to function as a detective in a precinct. Physicians who excel at CPC's are not necessarily good clinicians. A CPC has nothing in common with clinical medicine, because the CPC conductor sins against the fundamental concept in medicine that nobody should ever give an opinion about a patient he hasn't examined himself. All this notwithstanding, a CPC is an excellent educational exercise mainly for the physician who, so-called, conducts it.

Dr. Ty:—Since there is question about the distal end of the stomach, I should like to clarify it verbally. The lesion seen in this portion of the stomach is well circumscribed, radiolucent, and persistently seen during fluoroscopy. There is no thickening of the rugal pattern or any ulcer crater seen.

Dr. Snapper:—No destruction of the rugal pattern? Then I think we are justified in diagnosing this as a carcinoma of the stomach. It must be a leiomyoma, a lipoma or a neurofibroma.

Dr. Wangensteen:—He couldn't die of that.

Dr. Snapper:—This lesion is only emphasized to make our task more difficult, I would surmise.

Question:—Do you think it has nothing to do with the benign lesion, not having to do with the rest of it?

Dr. Snapper:—I think so.

Question:—Would you comment on the fact it has been nonsplit fatty acid and will be split by bacteria in the bowel, and then produced?

Dr. Snapper:—I gladly will.

If a patient has a pancreatic carcinoma, or pancreatitis, the fatty acids are not hydrolized; therefore, in the small intestine no fatty acids are present, and no calcium soaps are formed. Therefore the absorption of calcium is not impaired. When the nonhydrolized neutral fat passes the ileocecal valve into the colon, the bacteria of the colon can and will hydrolize the fatty acids. Thus in the colon calcium soaps will be formed,—but only from the calcium which had already reached the colon. Since calcium is not absorbed from the colon anyway it makes no difference whether *in the colon* the calcium is present as a calcium soap or as calcium phosphate because it is not absorbed in either form.

As is usual in medicine exceptions exist. All this holds true for the normal intestine; however, in fatty diarrhea the ileocecal valve is usually not competent and bacteria may penetrate in the lower part of the small intestine. These bacteria can split neutral fats; the resulting calcium soaps are not absorbed and thus even in fatty diarrhea due to pancreatic disease there is sometimes excessive calcium in the stool. Nevertheless, the differences between the different forms of fatty diarrhea are well illustrated by the following experience. Children with fatty diarrhea due to Gee-Herter's or celiac disease, suffer from severe rickets, children with fatty dairrhea due to cystic fibrosis of the pancreas never suffer from rickets.

Question:—We heard last year in this course that calcium zones are the things that make that so-called deficiency pattern. I think that Dr. Crohn's personal roentgenologist said in one of the lectures he sees a deficiency only if he has calcium zones. It is written up in our journal, on the small bowel.

Dr. Snapper:—I am not responsible for what Dr. Marshak says.

Dr. McKittrick:—Are there any other questions? Dr. Wangensteen, do you have anything to add?

Dr. O. H. Wangensteen:—Just a couple of things in this surgical guessing game: I cannot help but think that the stomach contains a lesion. It could be a leiomyoma and, if that is the primary cause of death, it should then be a leiomyosarcoma.

I know very little about sprue, but what I know about sprue suggests that the situation under consideration could conform to such an entity. It is certainly not tuberculosis of the small gut, I would say. The likely thing would appear to be a primary malabsorption phenonemon of some sort. This chap also apparently had a chronic cardiac lesion of some sort.

Dr. Snapper:—Chest normal as far as I can see. A carcinoma of the left lower lobe, however, is not visible in the routine A.P. exposure. On the other hand carcinomatous infiltration of the mesenteric lymph nodes is nearly always due to carcinoma of the stomach or of the intestine.

Dr. Wangensteen:—Apropos of Dr. McKittrick's question, my experience would conform to what I think he was trying to point out, that you do not get much infiltration of many lymph nodes in the mesentery in carcinoma without having peritoneal fluid. There was no suggestion of peritoneal fluids in this instance.

Dr. Snapper:—It certainly is not a myeloma.

Dr. McKittrick:—Dr. Meissner, why don't you take him off the hook?

Fig. 1—Gross photograph of typical appearance of the intestinal mucosa. Note the accentuation of the villous pattern.

Dr. William A. Meissner:—Dr. Snapper, I congratulate you. This is not a case of myeloma. (Laughter)

The findings at autopsy, other than the generalized extreme emaciation, were limited essentially to the gastrointestinal tract. In the pyloric end of the stomach there was a lipoma which was 2.5 cm. in diameter. The nodes of the mesentery and those about the abdominal aorta were considerably enlarged, but discrete; they did not grossly suggest malignant tumor. The mucosa of the entire small intestine appeared villous, resembling the nap of a rug (Fig 1). Thickening of the intestinal wall was limited primarily to the mucosa and submucosa. The cecum showed a slight edema, but the remainder of the large intestine was unchanged.

Microscopically, the small intestine showed villi which were crowded with large, foamy cells appearing like macrophages filled with fat (Fig. 2). This resulted in an overaccentuation of the villous pattern of the small intestine. These large cells contained foamy cytoplasm which stained positively with Schiff stains, but not with fat stains. The lymph nodes of the mesentery and periaortic region were engorged with similar cells. Other organs of the body, including the pancreas and liver, were microscopically normal.

Our diagnosis in this case was Whipple's disease, or intestinal lipoid dystrophy. The cause of this disease is obscure. When described by Whipple in 1907 it was thought to be due to a lipoid disturbance–hence the term lipodystrophy.

We have withheld one bit of information which would have been very helpful to Dr. Snapper. This case has been reported in the *Journal of the*

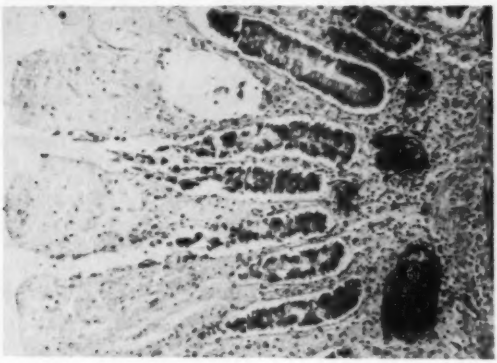

Fig. 2–Photomicrograph of intestinal mucosa showing the presence of the large cells with foamy cytoplasm in the villi, accounting for the accentuation of the villous pattern. (x200)

American Medical Association, 23 May 1953, as the 42nd case of Whipple's disease and one of the five cases diagnosed before death.

Dr. McKittrick:–Any comments, Dr. Snapper?

Before you make any comments, may I commend you for a good discussion of what proved to be the correct diagnosis–I so frequently don't even mention the right one.

Dr. Snapper:–It was evident that the fatty diarrhea was not due to sprue or to a pancreatic disease. Therefore it was probable that an infiltration of the mesenteric nodes, blocking the lacteals was present! It was difficult to pinpoint the infiltrating disease. In the absence, however, of convincing evidence of a carcinoma or Hodgkin's disease, a granuloma, like Whipple's disease,–the latter affecting the wall of the small intestine and the lymph nodes–seemed to be a reasonable possibility.

Dr. McKittrick:—Thank you very much. That was really an excellent discussion.

Dr. Wangensteen, would you like to take over now?

Protocol—II

This 62-year old male was admitted with the chief complaint of vomiting. About two years ago he began to have episodes of vomiting of bilious material and food residues. The vomitus was often "very acidic". The vomiting became progressively more severe and after a few months (20 months prior to the present admission) he was admitted to another hospital where x-rays were said to suggest pyloric obstruction. An exploratory laparotomy was carried out but no definitive surgery was done. Following that hospitalization the patient was free of symptoms for three months, but the vomiting gradually recurred and became progressively severe, so that recently he has had severe discomfort, causing him to reduce his diet to bland foods, and for the past few days only fluids. He has never had hematemesis or melena. No epigastric pain at any time.

Past history, family history, and history by systems, noncontributory.

Physical examination:—Temperature 98.6°, pulse 70, respirations 20, blood pressure 108/70. Patient appeared emaciated and had a dry skin. Lungs negative. Heart revealed a Grade II apical systolic murmur and occasional extrasystoles. Abdomen soft, no palpable masses, tenderness or spasm. Liver not palpable. Rectal examination negative.

X-rays showed normal esophagus and stomach. Duodenum was dilated down to the third and fourth portions. The fourth portion showed constant narrowing with loss of normal mucosal pattern. No definitive evidence of ulcer crater and no characteristic margin of tumor.

Laboratory Examination

Routine urine	Normal
Hemoglobin	8.8 gm.
White blood count	9,600
Differential	Normal
NPN	27 mg.
Chlorides	89 mEq.
CO_2	35 mm.
Sodium	140 mEq.
Potassium	3.2 mEq.
Gastric Analysis:	
Free acid	82°
Total	111°
Blood	2+
Cytology examinations of gastric contents	Unsatisfactory
Stool guaiac	2+

After suitable preparation for surgery, an operation was performed.

Dr. Wangensteen:—I was handed this memorandum by Dr. Meissner, a few minutes ago, I confess I have not studied it and have just skimmed through as we have been sitting here. My experience has been that the ear is better than the eye in these analyses.

Shortly after the Pilgrims came to Boston in this area two and a half centuries ago, a practice began of putting people in the stocks for offenses real and imagined and they have been doing it with professors on occasions like this ever since. In Nathaniel Hawthorne's immortal Scarlet Letter, the villain, the Reverend Dimmesdale, became a hero to the reader only after he had mounted the pillory and stood in the stocks with Hester Prynne and his unacknowledged child, Pearl, beside him.

Exhibiting the diagnostic defections of professors is still a frequent pastime of pathologists. It is a practice which may continue well beyond the twentieth century, because it is a facet of human nature to see our friends and heroes in the stocks.

The 62-year old man of this story was admitted with the chief complaint of vomiting. About two years ago he began to have episodes of vomiting of bilious material and food residues. The vomitus was often "very acid". The record states that the total gastric acid was 32 degrees.

The patient had been admitted to another hospital for x-rays, which were said to suggest the presence of pyloric obstruction. The roentgenologist can, of course, be confused as to where the pylorus is. They do not like to have you say this, but even the surgeon at times cannot always readily find the pylorus with the belly open.

We are told that an exploratory laparotomy was carried out, but no definitive surgery was done. That could have been so for two reasons: 1. Because no lesion was found, and 2. because the lesion was irremovable. Following that hospitalization, the patient was free of symptoms for three months; however, the vomiting gradually recurred and became progressively severe, so that recently there had been great discomfort causing the patient to restrict his diet to bland foods, and for the past few days to only fluids. There had never been hematemesis, melena, nor epigastric pain.

The past and family history as well as the history by systems, we are told, are noncontributory.

On physical examination, the patient apeared emaciated and had a dry skin. The lungs were negative. The heart revealed a Grade II apical systolic murmur and occasional extrasystoles. The abdomen was soft; there were no palpable masses; neither tenderness nor spasm were elicited. The liver was not

palpable. The rectal examination was negative. The temperature was 98.6°; the pulse 70; respirations 20; the blood pressure was 108/70.

X-ray studies showed a normal stomach and esophagus. The duodenum was dilated down to the third and fourth portions. I think we should see those x-rays, however. The fourth portion of the duodenum showed a constant narrowing, with loss of the mucosal pattern.

Dr. McKittrick:—Would you like to see the x-rays now?

Dr. Wangensteen:—Very well. With blood present in the stool and the story of vomiting and the disclosure of a deformity in the duodenum, one would think, of course, of a lesion in the duodenum. We shall, however, have to see the evidence to confirm the suspicion.

Dr. Ty:—(Slide) This is an area persistently seen during fluoroscopy, and in all films, which is narrow and proximal to this portion. The first and second portions of the duodenum were dilated.

Dr. Wangensteen:—This little deformity on the distal duodenum—was it present in all the films?

Dr. Ty:—You mean this one here?

Dr. Wangensteen:—Just beyond.

Dr. Ty:—Not present. It is normal.

Dr. Wangensteen:—Do we have other films?

Dr. Ty:—I have a spot film which shows the narrowing area in both portions, and this is the stomach pattern, which is normal.

Dr. Wangensteen:—Any other films?

Dr. Ty:—We just have two films.

Dr. Wangensteen:—The laboratory data otherwise are not really very interesting. I would think two possible diagnoses are in order. I would consider first, cancer of the duodenum with a stricture in this area. With a low hemoglobin and blood in the stool, I would favor the diagnosis of cancer of the duodenum. I suppose the surgeon might not have felt it because that portion of the duodenum is not easily palpable, without making a special effort to do so.

Dr. McKittrick:—Would you like a report on the operation?

Dr. Wangensteen:—I would like to state the other possibility that occurs to me, as I interpret the situation—that of a congenital membrane in the duodenum. Such a situation could explain why the surgeon failed to find a lesion. Now, a patient with membrane in the duodenum does not often live to be 62 years of age without prior surgery. I have, however, seen a patient with such a

lesion late in adolescence, and I believe several instances have been reported where patients have gotten into their more mature years with a membrane which obstructed periodically in the duodenum, before coming to surgery. If the two films we saw are representative of the situation in the duodenum, I am not very much impressed with the dilatation of the duodenum. If it were a membrane, we would expect to see the duodenum greatly dilated and large. Such is not the case.

One other thing—one reason I inquired if a filling defect could be seen in the first portions of the duodenum is that a cholecystoduodenal fistula might possibly be responsible for the duodenal deformity. It would be essential, however, that the gallbladder was overlying and in actual contact with the duodenum. I have seen gallstone ileus of the ileum with additional gallstone trapped in the retroduodenal duodenum. That situation can happen. There was no stone here and no suggestion of an antecedent obstruction. The duodenojejunal angle is apparently quite a difficult hurdle for a large gallstone to negotiate if it finds its way into the duodenum through a cholecystoduodenal fistula. A large stone can apparently remain in the retroperitoneal duodenum for a long time. When it has passed the duodenojejunal angle, it is likely to become arrested in its descent, obstruct temporarily and move on again, finally becoming impacted in the lower reaches of the ileum.

We have been told and we have observed in the x-ray films a filling defect in the third portion of the duodenum. This filling defect in the light of the history should be a cancer of the duodenum. That is my diagnosis on weighing the evidence presented.

Dr. McKittrick:—This happened to have been a patient of mine and I was a little confused by the study, especially the interval film. This was in January of 1956 that he had his first operation, and I saw him in my office in June of 1957, so a year and a half had intervened between the other operation and the time I saw him.

I will read you most of this letter:

"One week prior to admission the patient had a barium swallow which revealed a dilated stomach with only a trickle of barium passing through the duodenum. Laboratory studies revealed negative urine, hemoglobin 7.7 gm., normal NPN, total protein 5.2, albumin 4.75, and globulin 5.6 (I suspect an error there), sodium potassium 4.3. He was transfused and brought back to normal. The patient was explored with a tentative diagnosis of obstructing duodenal ulcer."

I know this will interest you:

"Examination of this patient was made with a Wangensteen's suction for several days. There was no evidence of any ulcer present in the second portion of the duodenum."

Now, it is a little hard to put that with the x-ray report above.

"There were numerous adhesions between the duodenum and gallbladder. The gallbladder was entirely negative other than the firm adhesions present. The common duct was negative and the head of the pancreas was negative. There was no posterior gastric or duodenal ulcer present. The liver was negative. The entire small bowel and large bowel were investigated and nothing abnormal was found. There were a few glands in the mesentery of the small bowel such as one would find in mesenteric adenitis in a youngster, enlarged nodes in the transverse mesocolon, some of which were calcified; there was no Meckel's diverticulum.

"In view of the obstructions on the x-ray, the second portion of the duodenum, the pancreas was further investigated. The head was found to be slightly enlarged, however, it felt normal to palpation. A biopsy of the pancreas was taken, and one of the mesenteric nodes was excised preoperatively.

"He did well and was discharged on 31 January. That was about three weeks after he came in. I saw him a few months after discharge and he was fine. The pathological report: hyperplastic lymph node with some subacute inflammatory reaction. The pancreas tissues were normal.

"The patient signed out with a diagnosis of mesenteric adhesions, etiology unknown—question mark: of tubercular origin. Chest plate was negative."

That was a year and a half before he came under my observation and, having been operated upon and being no better, he didn't respond very enthusiastically to my suggestion that he needed another operation. So it was from June until the middle of August before he finally came in, at that time really not being able to keep anything down. He came into the office with a big dilated stomach and succussion splash. This is a little information that isn't here in your record.

Dr. Wangensteen:—You are not withholding any x-ray films?

Dr. McKittrick:—No, no other films. There is something else I might say about the vomitus. Whatever they took out of his stomach was pea-green stuff, showing definitely the presence of bile. There was no jaundice.

Dr. Wangensteen:—Presumptive—it did not mention an ulcer. I have yet to see a duodenal ulcer in the fourth portion of the duodenum. Periodically one hears mention of such an ulcer, but it usually then concerns the Zollinger-Ellison ulcerogenic pancreatic tumor; but the bona fide garden variety of duodenal ulcer is within reach of the duodenal cap or a short distance beyond. I have never seen a duodenal ulcer beyond the papilla. There the neutralizing force of bile and pancreatic juice is such that a few centimeters beyond the duodenal contents will have a pH that is in the area of 4.5 or 5. A duodenal ulcer in this area therefore would seem very unlikely.

The differential diagnosis, I would think, would lie essentially between a cancer of the duodenum and a duodenal membrane; yet, if it had been a membrane, one would think this chap would have vomited periodically throughout his life, and we did not see any evidence of a megaduodenum in the x-rays.

Dr. Wm. Ladd, of the Children's Hospital here in Boston, long years ago described external extrinsic duodenal stenosis–a complication in which adhesions obstruct the third or fourth portions of the duodenum. Most of us have seen this condition and it usually concerns young children. These children sometimes reach adolescence before symptoms supervene which compel surgical interference. There is always an enormously dilated duodenum, as big as the stomach itself. This duodenum to me did not look extraordinary and the pictures we have seen are representative of the duodenum. I believe we can exclude duodenal stenosis as well as a duodenal membrane. My diagnosis therefore is cancer of the duodenum.

Dr. McKittrick:–Dr. Wangensteen, Dr. Meissner has been asking me about the improvement after an operation at which nothing was done. When he came into my office with a big, dilated, distended stomach, he was so skinny you could have seen an olive in there. I have forgotten how much fluid he had in his stomach but after it had been kept empty for 48 hours, the signs of obstruction let up quite markedly, and he was able to take a reasonable amount of food and have relatively little residual in his stomach. He really was not completely obstructed.

Dr. Wangensteen:–Dr. McKittrick is suggesting that we consider the possibility of an arteriomesenteric ileus. No one readily understands the mechanism by which the third portion of the duodenum becomes compressed by the mesentery of the small intestine.

Staveley, of Pittsburgh, I think, described a duodenojejunostomy for the relief of arteriomesenteric ileus in 1910. The operation, I feel, has very few indications and rarely needs to be performed.

Bloodgood (1912) suggested right-sided hemicolectomy to lessen the drag of the mesentery upon the duodenum.

If there is an intrinsic narrowing at this level–it must be an intrinsic lesion –an ulcerating, stenosing, carcinoma would most likely explain the situation.

I have not done any short-circuiting operations for arteriomesenteric ileus. I think the situation is very much like that of spastic ileus. Some day one learns the true diagnosis. Spastic ileus and arteriomesenteric ileus are essentially secondary phenomena, secondary to some obscure condition. I do not know whether Dr. McKittrick is trying to prepare us for the acceptance of such a situation such as arteriomesenteric ileus; however, in the light of the filling defect and the blood in the stool, I think one would have to rest the case on

an intrinsic neoplastic lesion in the duodenum rather than on extrinsic duodenal compression.

Question:—How about regional enteritis?

Dr. Wangensteen:—I am very limited in this area. I know that Crohn, who described regional enteritis pointed out that the lesion could occur in the duodenum. I have seen x-ray pictures of patients who have regional cicatrizing enteritis whose films suggest the presence of a concomitant duodenitis; however, I have seen no strictures with ulceration at that level. Have you seen duodenitis at this level?

Answer:—No, I haven't. I have heard about it.

Dr. Wangensteen:—Without lesions lower in the bowel?

Answer:—It has been reported.

Dr. Wangensteen:—Perhaps more often as a component of regional ileitis?

Question:—You haven't seen it?

Dr. Wangensteen:—Yes, I have seen duodenitis in patients with regional ileitis, but I have not seen a stricture in the retroperitoneal duodenum.

Dr. McKittrick:—Another surgeon went over his small bowel, and he found nothing in it. That is all we know. We have that information.

Dr. Wangensteen:—I should be grateful for any other suggestions.

Dr. Snapper:—Dr. Helmuth Nathan, several years ago, in our Postgraduate Course, stressed the clinical importance of paraduodenal hernias. Maybe an internal hernia could be considered in this case.

Dr. Wangensteen:—I would think an internal hernia would be very unusual. It would have been manifestly unfair to have withheld a film showing dilatation of the small gut, which would of necessity have had to be present if this entire situation were explicable on the basis of a retroperitoneal hernia.

There are hernias in this area: right and left paraduodenal hernia; the right is rather uncommon and the left is more common—another internal hernia in this area is through the foramen of Winslow—all these have rather characteristic x-ray findings in the presence of obstruction and can be diagnosed preoperatively not infrequently from the character of the x-ray shadows.

Dr. Snapper:—I have had the remarkable experience of being permitted to make the diagnosis of a lipoma of the stomach. I realize that I should not tempt my luck by diagnosing a paraduodenal hernia.

Dr. McKittrick:—Couldn't you almost exclude the hernia on the basis of obvious blood loss, hemoglobin of 7.5 gm. when he came to the first hospital,

and around 8 gm., or whatever it was here, when he was admitted here? Wouldn't that almost rule out—and wouldn't the hernia be a more intermittent thing?

Dr. Wangensteen:—In paraduodenal hernias you get a suggestion of the bowel being contained in a sack with rounded contours laterally as well as below in x-ray studies of the small intestine. There are smooth lateral curves here but not so beneath. Hence this is not a paraduodenal hernia. Such hernias may exist, of course, without the presence of acute obstruction. It would be difficult to conceive of a hernia of the small intestine through the foramen of Winslow without acute bowel obstruction.

Dr. Snapper:—I didn't actually insist that the man had a hernia. I think he had an obstruction at the ligament of Treitz, probably by enlarged lymph nodes, either carcinoma or lymphosarcoma.

Was this patient ever put on his belly?

Dr. McKittrick:—No.

Dr. Snapper:—It is an old experience that in an arteriomesenteric occlusion, this position liberates the stomach and duodenum and the incessant vomiting stops. I hardly dare to add that 1 mg. of strychnine injected over the area of the stomach is also helpful.

Dr. McKittrick:—Are there any other comments?

Well, I suppose I have got to take the part of the pathologist here because, fortunately, this patient didn't go to Dr. Meissner.

We had the advantage, of course, that Dr. Wangensteen and Dr. Snapper didn't have, of really going over the x-rays with a radiologist and seeing the whole batch. From these you could not help but be convinced that the man had a lesion of the third portion of the duodenum, probably within the duodenum itself. The next helpful information was the character of his vomiting. The lesion had to be distal to the ampulla for him to have had the pea-green vomitus that he had. Our preoperative diagnosis was obstruction of the third portion of the duodenum, probably carcinoma.

The reason I thought "probably", was that I was disturbed by the interval of time. I saw him in June, and I thought he was going to starve to death and go into some sort of electrolytic imbalance and dehydration if he didn't have something done within a very short period of time. He refused. He said, "I have been operated upon. Who are you to make me any better, if you operate on me?" Then I just shrugged my shoulders. That was all I could do. I simply told him he needed help.

At operation the first thing that intrigued me was a dilated biliary tree without jaundice. I have often wondered whether jaundice comes first or

whether with a carcinoma of the ampulla the palpable gallbladder comes first. I had seen one previous patient who came into the hospital because of a palpable mass, who was neither clinically nor chemically jaundiced.

This patient had a big, distended gallbladder secondary to a carcinoma of the ampulla. She became jaundiced a few days after admission.

Dr. Wangensteen's patient had a mass in the third portion of the duodenum just distal to the ampulla—in fact now involving it.

We removed half or a little better of the pancreas, and did the regular Whipple procedure, carrying the removal down to the jejunum, so we took out

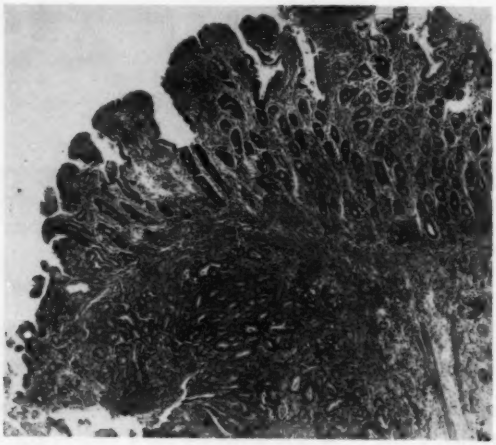

Fig. 3—The normal duodenal mucosa is above. The carcinoma is below and to the left. The pattern of the tumor is that of a primary intestinal carcinoma. (x50)

a little bit more of the small bowel than one would normally take out in doing a Whipple for a carcinoma of the head of the pancreas.

Fortunately, surgically he had a very satisfactory recovery. I wish you had been here, Dr. Snapper, because he had a terrible diarrhea for a while. That may or may not have been due to the loss of pancreatic secretions. It was not tracked down to the degree that this other case was, but all of it finally cleared up all right.

Dr. Wangensteen:—Did you ligate the pancreatic ducts?

Dr. McKittrick:—I never ligate the pancreatic duct, but put the end of the jejunum, or whatever it may be, into the end of the pancreas, and I don't put anything in the duct. I just leave it alone.

I am sorry to say that I really haven't followed nearly enough of these patients carefully with stool examinations, and so forth, to know whether the pancreas really functions or not. They get along surprisingly well and I suspect that it does.

Dr. Meissner:—The specimen received in the laboratory from Dr. McKittrick included the distal portion of the stomach, upper duodenum, head of the pancreas and a portion of the common bile duct.

There was no evidence of active or healed ulcer in the stomach or in the first portion of the duodenum. There was moderate dilatation of the duodenum in the first portion. Beginning just proximal to the ampulla was an ulcerating carcinoma extending for 6 cm. along the duodenal mucosa and causing a partial destruction of the ampulla of Vater. The tumor extended into the walls of the duodenum, but did not infiltrate either the pancreas or any of the other adjacent organs or tissues. The common bile duct was dilated to about three times the usual size.

Microscopically, the tumor was a carcinoma composed of intestinal type epithelium (Fig. 3). It appeared low grade and resembled many carcinomas arising from small or large intestines. There were 16 lymph nodes identified; none contained tumor.

Dr. McKittrick:—What about the lymph nodes?

Dr. Meissner:—Sixteen, all negative.

Dr. McKittrick:—I would suppose that the long duration of this thing, plus the absence of lymph nodes, and a smooth liver, would suggest that this man might have a very good prognosis.

Dr. Wangensteen:—Cancer of the duodenum has the best prognosis of all the conditions for which one does the Whipple operation—as good a prognosis in fact as in cancer of the biliary ampulla, which condition has a far better outlook than cancer of the pancreas.

One is tempted occasionally, when one has a small cancer of the duodenum, to do a local excision and anastomosis, but one should never do it without putting a catheter down through the common bile duct. The surgeon doing such an operation for the first time will be amazed to find that his excision has probably cut across the interstitial portion of the common bile duct as it goes through the duodenal wall, necessitating performance of a Whipple procedure.

I think Dr. McKittrick knew what he was about when he set out arbitrarily to do an intentional Whipple procedure. I was interested in what Dr. McKittrick said concerning the restoration. Actually, of course, this is an old operation. In this country we call it the Whipple operation. It was Willy Kausch in Berlin who first did the operation successfully (1912) with implantation of the pan-

creatic duct, following excision of the head of the pancreas for cancer. Whipple and his associates (1935) advocated ligature of the pancreatic duct in the excision to lessen the hazard of pancreatic fistula. Following the initial successes of Kausch, the operation fell into desuetude, largely because it was not easy to do. It was Whipple and his associates who rejuvenated the operation by advocating ligature of the pancreatic duct. It was the late Verne Hunt of Los Angeles who suggested readoption of the Kausch plan of implanting the pancreatic duct into the jejunum in the excision to lessen the digestive and nutritional problems which attend radical pancreatectomy. No surgeon today would deliberately ligate the pancreatic duct without making a real effort to reimplant it, attending excision of the duodenum for cancer or for a malignant lesion of the ampulla or the head of the pancreas. He would do it as Dr. McKittrick did it, which is essentially the operation which Kausch did almost 50 years ago.

I believe the experience of surgeons who have done this operation for cancer of the duodenum suggests that these patients do as well as any for which one does the Kausch-Whipple-Hunt operation for cancer of the ampullary region. The over all experience, I believe, indicates that of patients surviving operation for cancer of the duodenum approximately 50 per cent of them survive for five years. I would think therefore that the prognosis for this lesion is reasonably good.

Dr. McKittrick:—Dr. Wangensteen, Dr. Snapper, and Dr. Meissner, thanks to all of you from everyone here. We have all had an interesting time and if all of you have learned as much as I have, it has certainly been a very productive hour and a half.

PRESENT STATUS OF GASTRIC CYTOLOGY*

A Study of 60 Cases by the Chymotrypsin Method

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Cancer of the stomach accounts for about 15 per cent of deaths from malignancy in the U. S. It is generally admitted that roentgen examination is the most reliable method for detecting cancerous lesions of the stomach. Unfortunately, radiographic diagnosis is frequently too late for successful treatment of the lesion. Gastroscopy, likewise, although a valuable diagnostic aid, is limited in its usefulness, since it is a rather formidable procedure and because of several blind spots encountered in its use. In the differentiation between a benign or malignant lesion of the stomach, even direct visualization frequently defies a definitive answer to our problem. We are thus forced to look elsewhere in search for newer methods for detecting early malignancy of the stomach. The cytological study of the gastric content appears to offer definite additional diagnostic aid. A survey of the various methods employed, as well as our own experiences with some of these technics, form the basis of this paper.

Simple Aspiration

Since Papanicolaou devised the cytologic examination for cancer cells by special staining, more malignant lesions were discovered in the various system tracts at an earlier stage. The stomach, however, resisted this form of investigation, as material obtained by simple aspiration contained few cells, and those present were either partially digested by the acid pepsin in the stomach or mixed with extraneous material, making a diagnosis difficult and at times impossible. Thus, routine gastric aspirates gave only up to a 30 per cent positive correlation in proved malignancies of the stomach. In 1948, however, Ulfelder, Graham and Meigs, by using normal saline and lavaging the stomach, rapidly centrifuging and fixing the material thus obtained, reported an accuracy of 85 per cent in the diagnosis of 14 cases of gastric malignancy.

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Abrasive Technics

Panico balloon:—In order to obtain increased exfoliation of abnormal gastric cells and better preservation of their morphologic detail, Panico, Papanicolaou and Cooper introduced the abrasive balloon. In the first series of 70 cases in which this technic was employed by the authors, there were 33 patients in

TABLE I

Malignant Cases

Patient No.	Age	Sex	Acid	Diagnosis			
				Clinical	Radiologic	Cytologic	Confirmed Diagnosis
1	61	F	Achl	Ca Pancreas	Carcinoma	Pos.	Infiltrative Ca
2	77	F	Norm	Ca Stomach	Benign G. ulcer	Pos.	Malignant ulcer
3	40	M	Norm	Ca Esoph.	Ca Esoph.	Pos.	Ca Esoph.
4	63	F	Achl	Ca Stomach	Carcinoma	Neg.	Infiltrative Ca
5	75	F	Norm	Ca Stomach	Carcinoma	Pos.	Infil. Ca
6	67	M	Achl	Peptic Ulc.	Malignant ulcer	Pos.	Infil. Ca
7	87	M	Achl	Dyspepsia	Carcinoma	Neg.	Infil. Ca
8	69	F	Achl	Ca Stomach Recurrent Ca	Carcinoma	Pos.	Infil. Ca
9	68	F	Norm	Ca Stomach	Carcinoma	Pos.	Infil. Ca
10	59	M	Norm	Ca Stomach	Carcinoma	Neg.	Infil. Ca
11	68	M	Achl	Ca Stomach	Negative	Pos.	Infil. Ca
12	80	M	Achl	Dyspepsia	Carcinoma	Neg.	Infil. Ca
13	56	M	Achl	Ca Stomach	Antrum Ca	Neg.	Infil. Ca
14	57	F	Achl	Ca Stomach	Carcinoma	Pos.	Infil. Ca
15	56	M	Achl	Ca Stomach	Carcinoma	Pos.	Infil. Ca

whom a pathologic diagnosis had been established by surgery. In this group of 17 malignancies the balloon technic disclosed malignant cells in 14 and suspicion of malignancy in one additional case. This prompted us to employ the abrasive balloon technic. In a group of 50 patients with suspected malignant

lesions, there were nine cytologically demonstrated cases of gastric malignancy with no false positive findings. Our accuracy in this group study was 78 per cent.

Rubin's antral abrasive balloon:—In 1952 Rubin et al modified Panico's abrasive balloon by adding a mercury weighted tip to assure its entrance into the antrum. They reported an accuracy of 90 per cent in their studies.

McLean cytologic balloon:—This is another method.

Gastric brush:—In 1953 Ayre devised the "gastric brush". Its principle is to mechanically abrade mucosal surface cells by means of 2 winged brushes at the end of a rotating cable.

Recently Neiburgs modified the Ayre brush by substituting a series of nylon loops in place of the brush. These loops contain numerous knots which help to abrade the stomach and trap exfoliated material.

We have found the Ayre brush and Neiburgs' modification easier to pass and less time consuming than the abrasive balloons, but do not have a large enough group to report upon at this time.

Chymotrypsin Technic

Exfoliating cells in the fasting stomach lie protected from gastric juice by a mucous layer. Histochemical experiments by Benditt and French established the fact, that chymotrypsin at pH 5.3 is capable of removing a substantial quantity of polysaccharides from cartilage, without the protein digestion inherent to crystalline trypsin at a higher pH. Hence the mucolytic enzyme liquefies the mucous barrier without materially altering the form of the cells. Drs. Rubin and Benditt in 1955 introduced the lavage technic using a solution of chymotrypsin in 500 c.c. of 1/10 molar acetate, pH 5.6, the buffer being employed to maintain a constant pH during the procedure. Speed in collecting and processing is necessary, to minimize the possible digestion of the material, and to that end a portable centrifuge is brought to the bedside.

Method:—Since barium contamination interferes with the procedure, roentgen studies are to be avoided for several days. If there is no obstruction present, a simple overnight fast is adequate. Otherwise repeated aspiration is necessary the night before, to avoid food contamination of the cytologic material.

On the morning of the study, a Levin tube is passed through the mouth eliminating lubricants. The patient is encouraged to expectorate and blow his nose to avoid contamination with nasal, pharyngeal and respiratory epithelium.

After the fasting stomach is aspirated, a preliminary lavage with Ringer's solution is performed and then the enzyme lavage follows. The chymotrypsin solution is prepared immediately prior to use by adding 7 mg. of alpha chymo-

TABLE II

BENIGN CASES

Patient No.	Age	Sex	Acid	Diagnosis			
				Clinical	Radiologic	Cyto-logic	Final
1	69	M	Achl	Peptic ulcer	Neg.	Neg.	Anemia
2	78	M	Achl	Ca Stomach	Neg.	Neg.	Ing. Hernia
3	76	F	Norm	Peptic ulcer	Ca Colon	Neg.	Ca Colon
4	71	M	Norm	Ca Stomach	Neg.	Neg.	Ca Prostate
5	64	M	Norm	Dyspepsia	Neg.	Neg.	Bronchiectasis
6	73	F	Achl	Ca Stomach	Neg.	Neg.	Dyspepsia
7	70	M	Achl	Dyspepsia	Hiatus hernia	Neg.	Ca Lung
8	75	F	Norm	Peptic ulcer	Hiatus hernia	Neg.	Hiatus hernia
9	72	M	Norm	Ca stomach	Hiatus hernia	Neg.	Hiatus hernia
10	64	M	Norm	Peptic ulcer	Hiatus hernia	Neg.	Hiatus hernia
11	38	M	Norm	Ca stomach	Carcinoma	Neg.	Dyspepsia
12	65	M	Hyper	Ca stomach	Pyloric obstruction	Neg.	Duodenal ulcer
13	69	F	Achl	Ca stomach	Neg.	Neg.	Dyspepsia
14	57	F	Norm	Ca stomach	Hiatus hernia	Neg.	Hiatus hernia
15	81	M	Hyper	Gastritis	Benign ulcer	Neg.	Benign G. ulcer
16	76	M	Norm	Ca stomach	Duodenal ulcer	Neg.	Duodenal ulcer
17	69	M	Hypo	Dyspepsia	Benign G. ulcer	Neg.	Benign G. ulcer
18	57	F	Norm	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
19	62	F	Hypo	Hiatus hernia	Hiatus hernia	Neg.	Hiatus hernia
20	66	F	Norm	Dyspepsia	Antral Ca	Neg.	Gastritis
21	69	F	Norm	Ca stomach	Hiatus hernia	Neg.	Hiatus hernia
22	70	F	Achl	Pernicious anemia	Benign G. ulcer	Neg.	Benign G. ulcer

TABLE II *(cont'd)*

Patient No.	Age	Sex	Acid	Diagnosis			
				Clinical	Radiologic	Cyto-logic	Final
23	68	M	Norm	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
24	71	F	Hyper	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
25	74	M	Achl	Peptic ulcer	Malignant ulcer	Neg.	Benign G. ulcer
26	49	F	Norm	Dyspepsia	Neg.	Neg.	Dyspepsia
27	59	F	Norm	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
28	78	M	Hypo	Peptic ulcer	Negative	Neg.	Dyspepsia
29	74	F	Norm	Dyspepsia	Negative	Neg.	Ca pancreas
30	70	F	Norm	Ca stomach	Duodenal ulcer	Neg.	Duodenal ulcer
31	67	M	Norm	Ca stomach	Negative	Neg.	Lymphoma
32	66	F	Achl	Ca stomach	Ca stomach	Neg.	Splenomegaly
33	72	M	Achl	Peptic ulcer	Negative	Neg.	Ca pancreas
34	68	F	Norm	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
35	42	F	Hyper	Peptic ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
36	73	M	Hyper	Gastric ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
37	63	F	Achl	Pernicious anemia	Negative	Neg.	Pernicious anemia
38	27	F	Norm	Dyspepsia	Gastritis	Neg.	Gastritis
39	53	M	Achl	Benign G. ulcer	Malignant ulcer	Neg.	Benign G. ulcer
40	60	M	Hyper	Dyspepsia	Benign G. ulcer	Neg.	Benign G. ulcer
41	70	F	Hyper	Benign G. ulcer	Benign G. ulcer	Neg.	Benign G. ulcer
42	51	F	Achl	Ca pancreas	Negative	Neg.	Ca colon
43	68	M	Achl	Peptic ulcer	Hiatus hernia	Neg.	Hiatus hernia
44	60	F	Achl	Ca stomach	Negative	Neg.	Ca colon
45	45	F	Hyper	Peptic ulcer	Duodenal ulcer	Neg.	Duodenal ulcer

trypsin to 500 c.c. of the 1/10 molar acetate solution. It is instilled into the Levin tube with the patient in the supine position. The patient is then rotated slowly through 360 degrees. After 10 minutes, aspiration is performed as quickly as possible. The collected specimens are kept on an ice bath prior to placing them into the centrifuge. The last aspiration is completed in the left lateral decubital position. The material is then centrifuged for about 3 minutes at 5,000 r.p.m. and the sediment is immediately smeared out and fixed in equal parts of 95 per cent alcohol and ether. At the most, 10 minutes elapse between aspiration and the fixation of cells. Within a half-hour the slide is ready for staining by the Papanicolaou method.

Rubin originally subjected a group of 64 possible cases of gastric malignancy to the chymotrypsin lavage technic. Of the 20 proven cases in the series, 19 were detected by this method. These exceedingly good results, however, have not been duplicated. Klayman and his co-workers diagnosed 60 out of 75 tumors correctly, but there were two false positives in their series.

TABLE III

ANALYSIS OF THE 45 BENIGN CASES

Diagnosis	Malignant	Benign
Radiologic	5	40
Cytologic	0	45

Crozier et al subjected a group of 122 patients to the lavage technic. Of the 29 eventually proved cases of malignancies of the stomach, 20 were recognized by the cytologic method. In the later phase of their study, however, their findings showed a better correlation.

Our reported series (Tables I and II) consists of 60 problem cases which were chosen at random from the wards and private services at the Jewish Hospital. Of the 15 malignancies ultimately proven by either surgery or autopsy, 10 were accurately diagnosed by the chymotrypsin technic or a 67 per cent correlation. There were no false positives.

Although this series is relatively small, it presents some interesting observations. Two of the cytologically proved positives had been undiagnosed by radiology or gastroscopy. Of the 45 established benign cases, 5 were erroneously diagnosed as malignant by radiology or gastroscopy. In contrast, the cytologic diagnoses were 100 per cent correct (Table III).

The following case reports emphasize the diagnostic aid of this method.

Case 1:–C. G., 40 yrs., male, admitted 31 January 1956, complaining of dysphagia of 3 years' duration, during which time the symptoms had not increased in severity. He sustained a weight loss of 40 lbs. Gastrointestinal series in June 1955 at another institution was reported as negative and the complaints were considered of neurotic origin. Patient was re-x-rayed at Jewish Hospital in 1955 and gastrointestinal series again was inconclusive. He was admitted with the diagnosis of chronic pyloric obstruction due to peptic ulcer or gastric malignancy. Chymotrypsin lavage on 2 February 1956 revealed malignant cells,

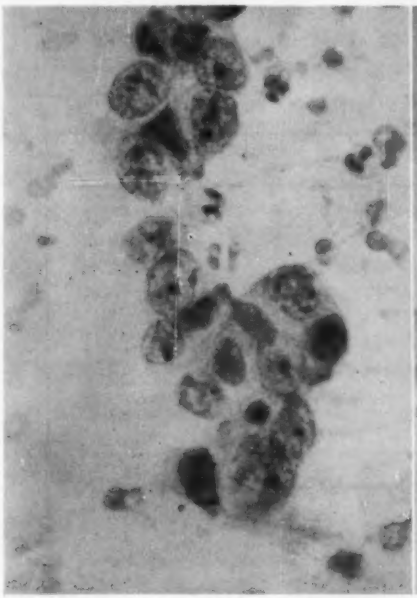

Fig. 1

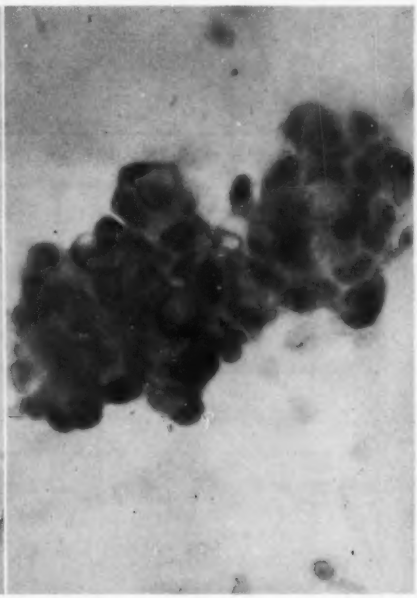

Fig. 2

Fig. 1–(P6765) High power. Nuclei variable in size and shape, many with prominent nucleoli, some hyperchromatic.

Fig. 2–(P7552B) High power. Malignant cells with deeply staining nuclei some of which are crescentic and markedly irregular in shape.

of the squamous type which suggested the possibility of an esophageal lesion. Study of the esophagus performed thereafter by radiography and esophagoscopy finally established the definite diagnosis of a carcinoma in the middle third of the esophagus. Scalenus node biopsy revealed metastases.

Comment:–This patient's complaints were first considered neurogenic in origin. Later a diagnosis of stenosing juxtapyloric peptic ulcer was suggested. Finally, however, cytologic study demonstrated malignant squamous cells which led to the true diagnosis of esophageal malignancy.

Case 2:—E. S., 74 yrs. History of epigastric pain with radiation to the back relieved by alkalis and food. Free acid was present in fasting stomach. X-ray report was "lesion on lesser curvature and suspicious mass in fundic region—possible malignancy." Gastroscopy on 31 October 1956 was diagnosed as gastric carcinoma. Chymotrypsin study 29 October 1956 was negative for malignancy. Surgery performed 2 November 1956 and no malignancy found.

Comment:—Both x-rays and gastroscopy conveyed the impression of a carcinoma of the stomach. Surgery confirmed the negative result obtained by the chymotrypsin technic.

TABLE IV

COMPARATIVE STATISTICS

Reference	No. of cases	Correct %
Malignant cases		
Klayman et al	75	80
Cooper et al	45	73
Cooper and Papanicolaou	51	74
Rubin et al	42	83
Fishman and Terzano	18	72
Present Study	15	67
Benign cases		
Cooper et al	155	94
Cooper and Papanicolaou	187	94.5
Rubin et al	69	96
Fishman and Terzano	30	90
Klayman et al	78	96
Present Study	45	100

Case 3:—Mr. D., #412705, was admitted to hospital (February 1957) with a 24-year history of upper abdominal pain and 27-year history of duodenal ulcer. During this admission there was x-ray evidence of a chronic duodenal ulcer and a possible benign gastric ulcer.

Chymotrypsin study done on 4 April 1957 revealed malignant cells. Surgeon at operating table as well as the pathologist, on gross examination of the specimen, reported the lesion as benign. Careful microscopic search, however, revealed a tiny nidus of adenocarcinoma.

Comment:—A case of carcinoma *in situ* was diagnosed by the chymotrypsin technic stressing the potential of this method and the search and diagnosis of early malignancy of the stomach.

Conclusion

The results obtained with exfoliative gastric cytology by various methods indicate that a valuable aid to our diagnostic armamentarium has been added. Gastric cytologic studies used in conjunction with roentgenography and gastroscopy definitely increase the number of early diagnoses. In our experience we found the chymotrypsin technic to be least cumbersome and disturbing to the patient. The cells obtained by this method were less contaminated and morphologically superior to those yielded by either balloon or brush technics (Figs. 1 and 2). Our results were somewhat less impressive than those of other authors (Table IV). We believe that further improvement and experience with exfoliative cytologic technics will enhance the value of this procedure. This relatively simple method may prove to be a practical and inexpensive screening device for the detection of early gastric malignancy.

Summary

1. A survey of the various methods employed in obtaining exfoliative cytologic material from the stomach and their relative merits is presented.

2. Sixty diagnostic gastric problem cases were subjected to the chymotrypsin lavage technic.

3. Chymotrypsin lavage appears to be a relatively simple diagnostic aid which proved of value in about 67 per cent of our cases.

4. Exfoliative cytology in conjunction with radiologic and gastroscopic studies resulted in a high degree of diagnostic accuracy in gastric malignancy.

Acknowledgment

We wish to acknowledge the invaluable assistance given to us by Dr. A. Mackles, Associate Pathologist and Cytologist at Jewish Hospital of Brooklyn and Miss F. Strauss, B.A. for technical aid in our work.

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SOLITARY DIVERTICULUM OF THE ILEUM CAUSING INTERMITTENT OBSTRUCTION IN THE ILEOCECAL AREA

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Case Report

Patient, G. O., male, age 39.

History:—For the past three months, patient has complained of lower abdominal distress with occasional cramp-like pain in the right lower quadrant. Frequently in the past two months, there has occurred diarrhea, consisting of loose, watery bowel movements without blood. These episodes would last no

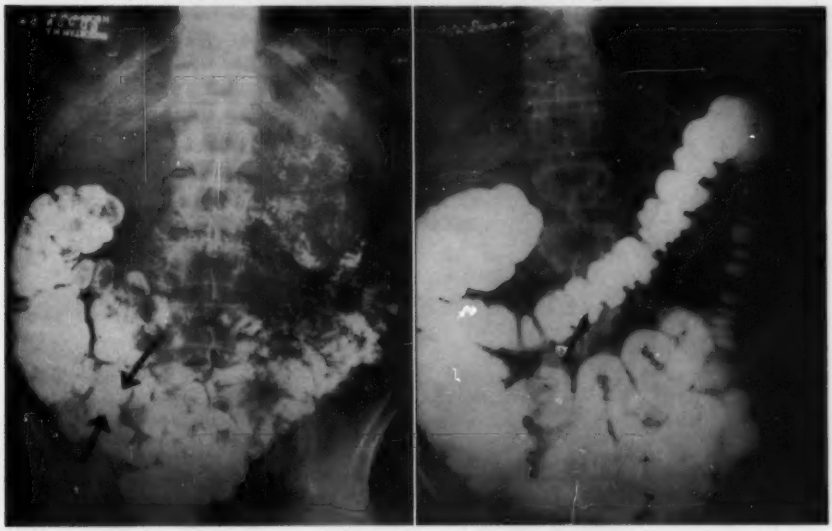

Fig. 1 Fig. 2

Fig. 1—Gastrointestinal series, one-hour film. The terminal ileum appears dilated, although barium passes freely into the cecum and the ascending colon.

Fig. 2—Barium enema. Arrow demonstrates an abnormality of the terminal ileum. 1. widening of the lumen, 2. an apparent filling defect, 3. suggestion of a pouch.

more than 24 hours with three to four successive bowel evacuations. Patient has never lost any time from his work or suffered any disability in his daily activities with the exception of some irritability caused by the recent annoyance of his abdomen.

Physical examination:—Reveals a fairly well nourished male adult, not acutely or chronically ill. Heart and lungs normal. There was no adenopathy noted. The abdomen was soft and no masses were palpable. Rectal examination revealed no masses.

Clinical impression was deferred and the problem was to rule out a lesion in the small bowel or the colon. Dr. Oscar Stern, the referring physician suspected clinically that there was pathology in the colon or the small bowel, possibly a neoplasm accounting for symptoms of partial intestinal obstruction.

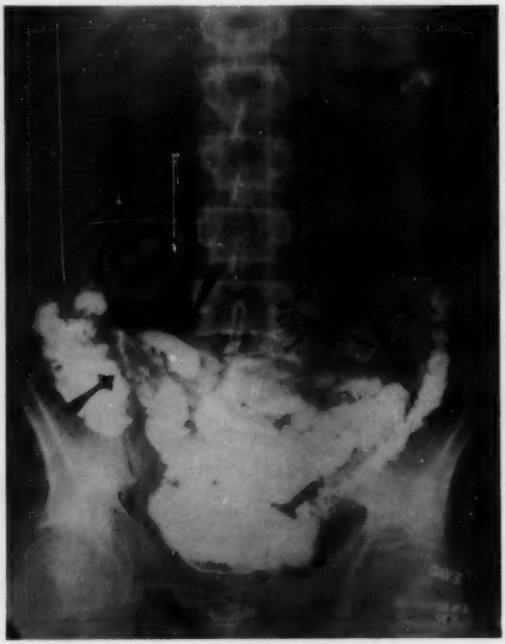

Fig. 3—Postevacuation, barium enema film reveals: 1. a large Meckel's diverticulum; 2. dilatation of the terminal ileum adjacent to the diverticulum.

Radiographic examination of the gastrointestinal tract by x-ray films and fluoroscopy reveals the following:

Esophagus:—No defects, no cardiospasm. Mediastinum clear.

Stomach:—Good tone, peristalsis active. No defects noted along the curvatures.

Duodenal bulb fills well. No ulcer craters or constant deformity demonstrable. Duodenal loop is not widened. Jejunum and ileum are normal in contour, motility and mucosal pattern except as follows:

The one-hour film (Fig. 1) in the gastrointestinal series reveals a slight dilatation of the distal ileum without demonstrating any detail of why this loop was distended.

Study of the colon by barium enema reveals no obstruction to the flow of barium to the cecum nor to the reflux of barium through the ileocecal valve into the ileum. Figure 2 revealed an abnormality in the appearance of the distal ileum. There is a bulbous dilatation of an apparent defect on the ileal side of the ileocecal area.

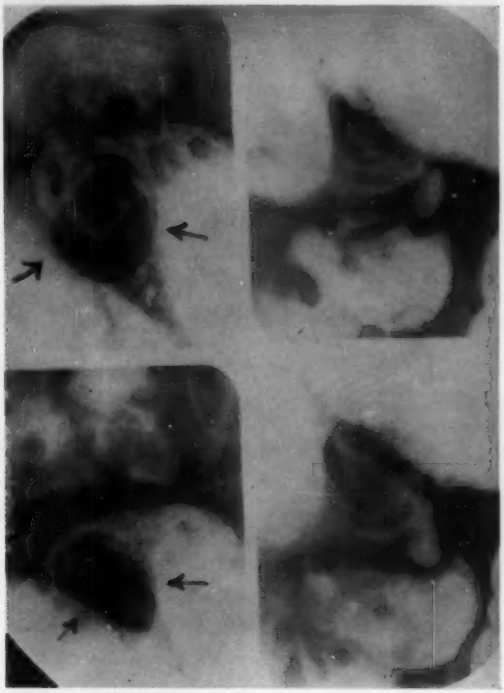

Fig. 4–Barium enema. Spot compression films in the area of the cecum reveals a large filling defect, round, measuring 3 cm. in diameter, smooth in contour.

The postevacuation film (Fig. 3) accentuated the appearance of the bulbous type of distention described in Figure 2.

Another postevacuation film (Fig. 4) revealed more clearly a sac filled with barium coming off the superior mesial border of the distal ileum. A narrow neck is also clearly demonstrated leading from the ileum into the diverticulum. In addition to the sac, an irregular translucent area (filling defect) is noted in the distal four inches of the terminal ileum.

Figure 5, representing spot compression films with graded compression, reveals a large oval filling defect in the cecum in the region of the ileocecal valve with an exaggerated conical extension of this filling defect.

Radiographic interpretation:—The positive abnormal findings were:

1. Moderate distention of the distal ileum noted on the one-hour film taken during the course of the gastrointestinal series.

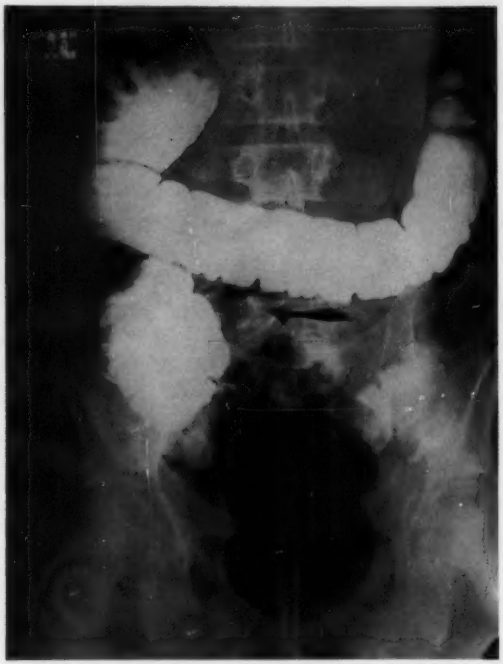

Fig. 5—Double contrast studies of the colon reveals air distended (Meckel's) diverticulum.

2. Diverticulum of the ileum, three inches in its base measurement, one inch in depth, connected by a narrow neck with the superior border of the distal ileum no more than one inch from the ileocecal junction. No niches or filling defects were noted within the diverticulum.

3. An irregular filling defect in the ileum adjacent to the diverticulum and noted at the same time that the diverticulum was demonstrated suggesting two independent lesions.

4. Filling defects (large) in the cecum in the area of the ileocecal valve on spot compression films.

The presence of a diverticulum of the ileum was obvious. The filling defects first noted in the ileum simultaneously with the demonstration of the diverticulum led us to believe that there are two independent lesions; diverticulum and tumor. The presence of a filling defect in the cecum made us speculate as to a third lesion. Undue prominence in size of the ileocecal valve with filling defects frequently suggest either tumor of the ileocecal valve or prolapse of the ileum into the cecum.

If there were no translucent areas in the ileum and no dilatation of the ileum proximally, a single diagnosis of diverticulum would be the most tenable one. A concomitant lesion, however, had to be postulated, namely a tumor of the ileum with intussusception into the cecum. Consequently, surgery was advised and the patient was operated by Dr. H. Mackler at the Madison Park Hospital of Adelphi College.

At the operation, a large diverticulum measuring two inches in diameter was found arising from the superior border of the terminal ileum, about four inches from the ileocecal valve. The diverticulum was ligated at the neck and removed.

Patient had an uneventful recovery and has been asymptomatic since the operation.

Conclusions

A patient having symptoms of intermittent small bowel obstruction is presented in whom a Meckel's diverticulum was noted radiographically. In addition, there was radiographic evidence that the diverticulum, by invagination and intussusception produced symptoms and signs of intestinal obstruction.

CORRELATION OF CLINICAL AND ROENTGEN FINDINGS IN UPPER GASTROINTESTINAL DISEASE

Report on 899 Cases

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The roentgenologist is frequently called upon to confirm a clinical diagnosis of a variety of upper intestinal disturbances. Since the clinical symptomatology of many diseases in this portion of the gastrointestinal tract may often be so similar in character, any attempt to differentiate such cases without the aid of the x-ray laboratory will be of no avail or at best leave a wide margin of doubt in the mind of the physician as to the accuracy of his diagnosis. Although the expressed need for roentgen studies in these patients is agreed upon, it is also recognized that the roentgenologist may not be able to offer a conclusive opinion[1].

In the present report we attempt to correlate certain clinical findings with the x-ray or fluoroscopic observations made over a 9-year period. It is clear to anyone engaged in this type of diagnostic work that close cooperation between the clinician who prepares the history with a tentative diagnosis and the roentgenologist who must use these to properly direct his study, is a highly important factor in arriving at a correct final diagnosis.

Method and Material

During the period covered by this paper 1,252 patients were studied by means of upper gastrointestinal barium meals with roentgen and fluoroscopic examination. Of this group only 899 were considered to have records which would properly lend themselves to this report. A total of 1,832 fluoroscopic examinations were performed in this group. No attempt was made to classify the diagnostic accuracy in terms of age groups, however, a racial classification is of some interest since there is approximately a one-third representation of three races as follows: white 241, Negro 249 and Indian 335. There were 74 patients of mixed racial strain.

In consideration of our results we defined an x-ray proven ulcer as a niche or crater demonstrable in 2 or more nonconsecutive exposures; a probable (or healed) ulcer as one in which a niche or crater was doubtfully demonstrated, or when a typical deformity or constant scar-like pattern could be demonstrated. A possible ulcer was considered when a tender or irritable duodenal cap was found or a reproducible distortion pattern could be delineated.

We have considered our findings as falling into two major groups, namely A and B. Group A consisted of those patients who gave a history of some forms

of gastrointestinal disturbance while Group B were those in whom no complaints referrable to the gastrointestinal tract could be elicited.

Results

In 840 cases (Group A) we were able to obtain a history suggestive of organic disturbance in the upper gastrointestinal tract. Of these our x-ray findings were confirmatory in 141 out of 230 of our ulcer group as shown in Table I.

Thus in 63.4 per cent the x-ray was to establish the diagnosis. An additional 17.8 per cent (41 cases) the x-ray findings strongly suggested that the clinical diagnosis was correct.

Of the 840 cases 16 were shown to have carcinoma, 3 esophageal, 9 gastric, 2 pancreatic and 2 small intestinal.

TABLE I

Roentgen Results in 230 Patients with a History Suggesting Ulcer

Ulcer Type	Total No.	Proven	Probable	Possible
Gastric	27	24	1	2
Esophageal	1	1	—	—
Duodenal	196	110	40	46
Marginal	6	6	—	—
Grand Total	230	141	41	48

Other diagnoses clarified by roentgen examination are shown in Table II.

In the remaining 529 patients of Group A we were unable to obtain any roentgen evidence of disease.

There were 59 patients who were placed in Group B. A summary of x-ray results in Groups A and B are shown in Table III.

In examining the records of the 529 cases of Group A wherever the roentgen findings were negative it was determined that the clinical diagnosis was fairly positive in 97, probable in 86, and uncertain in 346. In only 31 (5.8 per cent), however, did the clinical diagnosis point to an organic lesion of the upper gastrointestinal tract. These were atrophic gastritis 2 cases, epigastric hernia 1 case, and alcoholic gastritis 28 cases. The remainder of the group included lead poisoning, digitalis intoxication, amebiasis, bacillary dysentery, hepatitis, and extraintestinal disorders with symptoms referrable to the gastrointestinal tract.

The clinician was able to arrive at a quite definite diagnosis in 183 cases (97+86) without x-ray assistance. In 311 cases (91 per cent) out of 342 (311+31) possible opportunities, however, the roentgen findings were helpful in establishing a diagnosis.

Comment

As has been mentioned unless both x-ray and clinical findings are carefully integrated the diagnosis of gastrointestinal disorders may be left quite uncertain. It is evident that neither the x-ray nor the clinical history alone can be

TABLE II

Various Diagnoses Clarified by Roentgen Examination

Diagnosis	No.
Megaloesophagus	1
Short esophageal diverticula	5
Short esophagus	1
Esophageal varices	2
Diaphragmatic hernia	1
Hiatus hernia	16
Gastric syphilis	1
Gastric adhesions	2
Gastric polyp	1
Gastric diverticula	6
Gastric mucosal hernia without ulcer	7
Gastric malfunction	1
Gastric displacement by aneurysm	1
Pyloric stenosis	6
Duodenal fibroma	1
Duodenal polyps	2
Duodenal diverticula	10
Transposition of duodenum	1
Total	65

relied upon as being fully adequate. The history should always be considered as of prime importance and the x-ray as supportive or at best confirmatory. The 529 cases in this report bear evidence to the fact that symptoms cannot be ignored and should be used to assist the roentgenologist in helping the clinician be as accurate as possible. A few points in this regard were brought out when we directed our attention to the clinical history of the patients we examined.

1. Of 90 patients who had "ulcer-like" histories but also pain between awakening in the morning and breakfast, only 7 had proven or probable ulcer by x-ray.

2. Of 175 patients who had "ulcer-like" histories but no pain before breakfast 161 had proven or probable x-ray evidence of ulcer.

3. Of 182 x-ray probable or proven ulcer only 15 lacked the "ulcer history" or "past ulcer history" and of this group 132 described tenderness over an area of less than one inch in diameter.

4. Shift workers had approximately twice the number of stomach complaints and 4 times the number of ulcers per representative number of patients than did nonshift workers.

There may be certain limitations to the clinical histories utilized in the report as well as a failure to demonstrate certain lesions by x-ray. We have, however, presented our findings with reasonable assurance that the data presented offers worthwhile evidence to demonstrate the value to both patient and

TABLE III

ROENTGEN FINDINGS

No. Studied	Group A		Group B		Totals			
					Pos.		Neg.	
	Pos.	Neg.	Pos.	Neg.	No.	%	No.	%
899	311	529	0	59	311	34.6	588	75.6

physician in careful correlation of clinical history and x-ray findings in the diagnosis of disease of the upper gastrointestinal tract.

SUMMARY

The roentgen findings in 899 cases with gastrointestinal disturbance have been presented.

The diagnostic value of the x-ray has been given in some detail for 311 cases.

The importance of the history of no pain before breakfast and of the finding of a limited area of tenderness is stressed.

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ENDEMIC PSEUDOMEMBRANEOUS ENTEROCOLITIS IN HOSPITAL PATIENTS

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In recent months, clinicians have become aware of an increased incidence of enterocolic complications in patients after admission to hospitals. These have ranged in severity from mild, vague digestive disturbances, or transient diarrheas, to a severe fulminating, toxic cholera culminating in death.

As early as 1883, a fatal enterocolitis, eleven days after pyloric resection, was observed in Germany[1]. In 1939, 40 postoperative cases of fatal enterocolitis were reported for the preceding ten-year period. These deaths, at that time, were attributed to shock and vasomotor instability; bacterial infection was considered to play only a terminal role[1].

Since that time a changing concept has been evidenced in the literature, particularly with reference to the role of infection as a cause of morbidity and mortality. Foster et al[2], in a review of 5,190 autopsy records from the Lahey Clinic for the period 1928 to 1955, showed that infection played a major role in 24 per cent of these deaths. During the pre-sulfa era (1928-1937), in about ⅓ (34 per cent) of these deaths, infection was the major contributing cause. During the sulfa era this proportion was decreased to about ¼ (25 per cent). With the widespread use of antibiotics, a rapid decline to about 1/7 (14 per cent) was seen in 1946-1955. This proportion has been maintained, without any appreciable fluctuation, since that time. So it may be said that, in spite of the ever broadening spectra of therapeutic activity of the constantly growing list of new antibiotics and chemotherapeutic agents, one out of every seven deaths is still due to infection.

There is no longer a question of the development of a breed of infectious organism resistant to the wonder drugs. But, the question is raised as to the possibility that actual apathogenic strains may be so affected by these drugs, *in vivo*, as to enhance their virulence, changing them to pathogenic strains.

The *Staphylococcus aureus (micrococcus pyogenes)* has demonstrated an amazing ability to change characteristics, and a remarkable adaptability to adverse circumstances. These changes manifest themselves not only in the development of resistance to antibiotics and chemotherapeutic agents but also in ability to produce disease.

From 21 September 1957 to 21 December 1957, 36 cases of enterocolitis occurred in patients at St. Alexis Hospital, Cleveland, Ohio (Fig. 1). During the period studied the incidence of cases appeared in two separate phases. Thirteen cases had their inception during the first four weeks of the study.

During the following three weeks no new cases were recorded. Eight cases occurred in the eighth week and 15 developed sporadically to the termination of the study.

Of the 36 cases, only three occurred on floors devoted primarily to medical cases, and one occurred in a newborn, in the nursery. Eighty-nine per cent occurred in patients on floors devoted to surgical cases.

Sex distribution indicated 40 per cent higher incidence in males (21) as compared to females (15). Age distribution was commensurate with the age distribution of all admissions. Occupation and home residence did not evidence any epidemiological statistical significance.

Of the 36 cases of diarrhea, all but two received one or more of the antibiotics (Fig. 2). Ninety-five per cent of the diarrhea cases received one or more of the following drugs: penicillin, streptomycin, ilotycin, achromycin, terra-

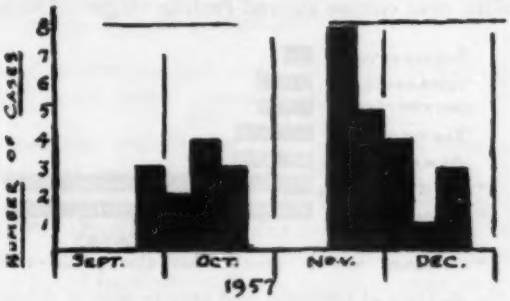

Fig. 1—Incidence of enterocolitis.

mycin, erythromycin and cathomycin before developing enterocolic symptoms. Eighty-three per cent of the group received more than one of these antibiotics. Within a period of five days following the institution of antibiotic therapy, more than two-thirds of these cases manifested their first signs of enterocolitis.

Of the 89 per cent of the cases of enterocolitis occurring on floors for surgical cases, 92 per cent were subjected to major surgical procedures of one type or another before the enterocolitis appeared. These procedures were as varied and nonspecific as one would expect to see on any daily surgical schedule.

Bacterial confirmation for *Staphylococcus aureus* was obtained with difficulty on blood agar until phenylethyl alcohol was used as an inhibitor for the overgrowing coliform organisms. From 29 such stool cultures, 19 (70 per cent) were found to have *Staphylococcus aureus* present. Pathogenicity of *S. aureus* is associated with the production of an exotoxin which coagulates blood plasma[3]. Chapman et al[4] in 1934 stated that of 690 pathological strains, 88 per cent

showed such coagulase activity. Surgalla and Dack[5], in 1955, in a study of 30 coagulase positive strains showed that they all produced a potent enterotoxin.

In our series of 19 confirmed S. *aureus* diarrhea cases 13 (70 per cent) had coagulase positive tests. Six control (nondiarrhea) cases, from the surgical floors, were also studied at that time using phenylethyl alcohol as an inhibitor. Two showed only the usual bowel bacterial inhabitants, *E. coli, Streptococcus fecales* and *Proteus vulgaris*. The other four showed S. *aureus*. Not one of these latter four showed any coagulase activity, being coagulase negative.

One of our cases is of particular interest and is typical. He was a poorly controlled diabetic with a gangrenous foot requiring mid thigh amputation. He was started on penicillin and streptomycin on the day of admission. Seven days later enterocolitis developed. All antibiotic therapy was immediately withheld. Diarrhea, toxicity and mental confusion persisted for about four weeks in a very severe form. Four days after admission, which was three days prior to the onset of his enterocolitis, stool culture showed *Proteus vulgaris*. During the first week

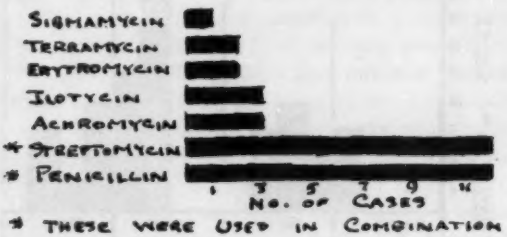

Fig. 2—Types of antibiotics used prior to onset of diarrhea.

of the diarrhea *E. coli* and *Pseudomonas aerogenes* were present. At the height of his enterocolitis, when he was having almost constant, bloody, watery stools, two cultures of coagulase positive *Staphylococcus aureus* were obtained. With abatement of the diarrhea in the fourth week, a culture of *E. coli* and coagulase negative S. *aureus* was found. With complete recovery and just prior to discharge from the hospital, stool culture once again showed *E. coli* only.

Turnbull[6] indicates the early signs and symptoms of postoperative enterocolitis: 1. diminished abdominal signs and distention, 2. tachycardia, fever and oliguria, 3. diarrhea and vomiting, 4. shock, toxic delirium, 5. leucocytosis and 6. fall in serum protein level plus anemia.[8]

In our series of coagulase positive S. *aureus* enterocolitis, this organism was found to be sensitive, *in vitro*, and responded *in vivo*, to the following antibiotics: neomycin, albamycin, furadantin and chloromycetin. From past experience we can anticipate that emergent strains will develop which will not be affected by these drugs.

The role of hospital infections with these organisms has recently been investigated in a one year study at Temple University Hospital[7]. Bacteriophage typing of *S. aureus* organisms showed that this organism was more than four times (69 per cent) as prevalent in hospital infections as in already ill patients being admitted to the hospital with *S. aureus* infections (16 per cent).

Of 265 nasal carriers of coagulase positive *S. aureus* among hospital personnel, only 4.1 per cent were infected due to organisms of this bacteriophage type. The role of the healthy nasal carrier is equivocal.

This same bacteriophage-type organism, however, was responsible for 76 per cent of the cutaneous abscesses acquired by patients during hospitalization, but not related to surgery, and also accounted for 80 per cent of the typed organisms from the cutaneous infections in hospital personnel. These were mainly in the form of pustules, paronychia and furuncles on exposed surfaces of the body such as forearm, hands and face. The frequently traced source of infection to the paronychia on the finger of the salad maker in outbreaks of *S. aureus* enterotoxin food poisoning, is classical.

The question of fomites and airborne transmission of pathogenic *S. aureus* is controversial and needs further investigation.

Austrian[8] noticed the similarity between pseudomembraneous enterocolitis and staphylococcus food poisoning. Bacteriophage typing of *S. aureus* etiologically responsible for staphylococcus enterotoxin food poisoning and the staphylococcus enterocolitis in hospital patients, shows both organisms are in the same group. In *S. aureus* food poisoning, the enterotoxin is introduced in a single dose in the contaminated food, therefore, the explosive onset of symptoms within a few hours, the termination within 24-36 hours, and the prostration for several days. Pseudomembraneous *S. aureus* enterocolitis may continue, however, as long as the predominate multiplying organism in the bowel lumen is the coagulase positive *S. aureus* producing its very toxic enterotoxin.

Summary

Thirty-six cases of endemic enterocolitis were observed over a period of three months during the latter part of 1957. A coagulase positive *S. aureus* was incriminated. There is evidence to indicate that hospital inmates, without enterocolitis, harbor apathogenic (coagulase negative) *S. aureus* in their stools, and that when these organisms become pathogenic (coagulase positive) the patient develops enterocolitis.

During the period studied, the majority of cases occurred in patients undergoing major surgical procedures of various types. All but two patients received antibiotics prior to the development of enterocolitis. Since the antibiotics are used with equal promiscuity on both surgical and medical patients, it may be

assumed that postoperative shock, anesthesia and electrolyte disturbances are factors in lowering host resistance to such infection.

The role of the cutaneous *S. aureus* carrier is important in the transmission of the infection.

The similarity of staphylococcus enterotoxin food poisoning and post-operative staphylococcus enterocolitis is noted.

Recommendations

1. Prohibition of promiscuous, unwarranted usage of antibiotics.

2. Maintenance of a high index of suspicion in all postoperative cases for the manifestations of enterocolitis.

3. Isolation of all enterocolitis cases occurring in hospital patients.

4. Contagious disease precautionary measures enforced with such isolation with particular attention paid to hand-washing, fingernail cleaning and bedpan sterilization.

5. Careful inspection of all hospital personnel, particularly those concerned with food-handling, for cutaneous *S. aureus* infection, by supervisory personnel.

6. Stool cultures and antibiotic sensitivity tests on all diarrhea cases—and the prescribing of only those antibiotics indicated.

7. The early administration of neomycin, albamycin, furadantin and/or chloromycetin, preferably by the intravenous route, while waiting for laboratory confirmation.

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USE OF FORTIFIED DEFATTED DRY MILK PROTEIN IN TREATMENT OF PEPTIC ULCERS

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The underlying causes of peptic ulcer are diverse and the etiological factors controversial. It is the accepted thought of numerous clinicians that the healing of a peptic ulcer can be accelerated when the environment at the site of the ulcer encourages the natural regenerative properties of the tissues. It was Sippy[1] who promulgated the thought that "the greatest hindrance known to the heal-

Fig. 1

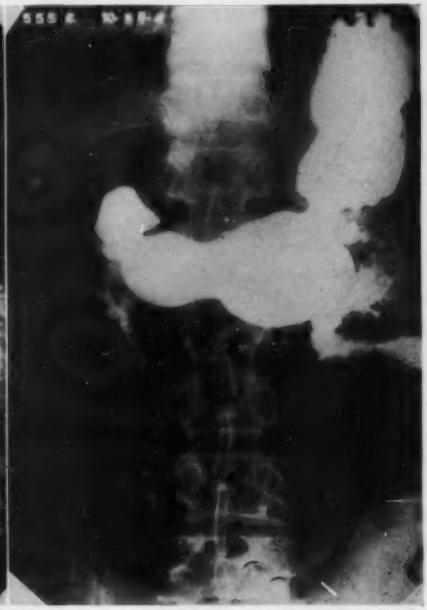

Fig. 2

ing of peptic ulcer is the disintegrating and digestive action of the gastric juice". It would therefore be most logical to create an environment at the site of an ulcer which would help neutralize this disintegrating and digestive action of the acid pepsin combination in the gastric juice.

In spite of the many new medications appearing on the medical horizons, the basis of our best approach to the problem of peptic ulcer therapy, is based on three predominant factors.

1. Suppression of gastric motor and secretory activity.

2. Alleviation of psychic stress and strain.

3. Improvement of nutrition in regard to protein.

Riese[2], recommends that "therapy must necessarily be directed toward the reduction of gastric acidity, protection of the ulcer crater and irritated mucous membrane, and the improvement of the patient's general health. Attempts

TABLE I

Results of X-ray Studies	No. of Cases
a. active duodenal ulcer	19
b. penetrating duodenal ulcer	3
c. duodenitis	5
d. gastritis	1
e. irritable colon	2
f. negative gastrointestinal tract	3

should be made to alleviate psychic stress by whatever practical measures the physician may be able to suggest in relation to the need for reassurance, possible environmental change, solution of personal problems and other approaches toward enhancement of morale. It must be remembered that psychotherapy alone has accomplished little material benefit for any substantial time".

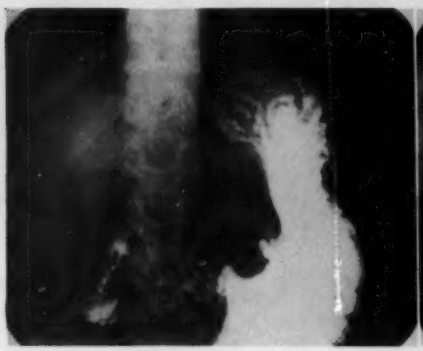

Fig. 3

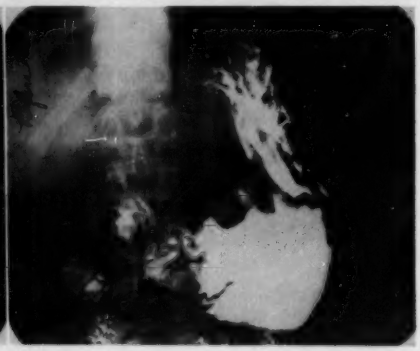

Fig. 4

It must be noted that neutralization or reduction of the acid chyme is extremely important and necessary in ulcer therapy. Many of our ulcer patients place themselves on restricted diets with the result that either they become deficient in calories, or in the necessary vitamins and minerals requisite to the rebuilding of body tissues and the peptic ulcer itself. The tissues are therefore

easily susceptible to nutritional disease and deficiencies. Many individuals are on a regime of drugs which disrupt the acid base balance of the body resulting in acid rebound or alkalosis.

Anticholinergics capable of reducing the secretory and motor activity of the stomach have proven unsatisfactory since they can also affect all the other organs supplied by the same nerves. Thus the secondary effects may be more unpleasant than any benefit obtained by their action on the upper gastrointestinal tract.

Sippyplex®* by its high protein, antacid content, B-complex, ascorbic acid and antihemorrhagic factor is a most logical and plausible product in the treat-

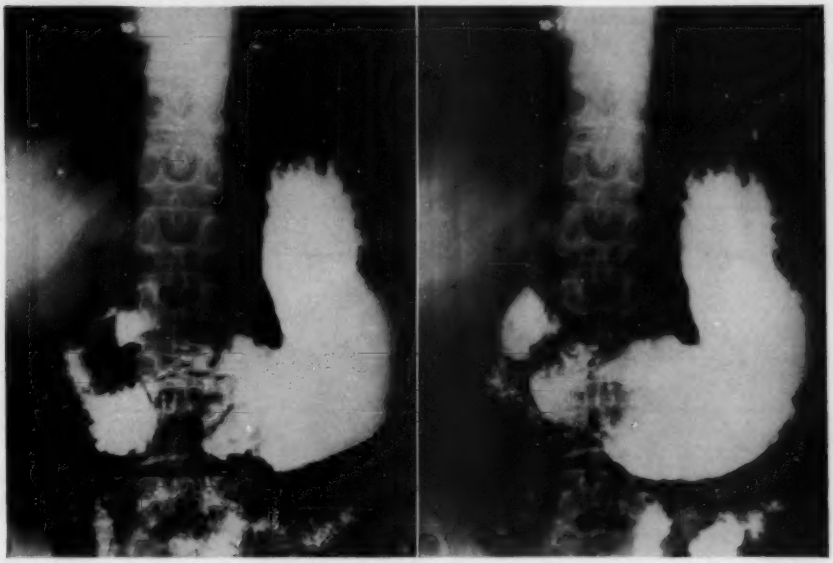

Fig. 5 Fig. 6

ment of peptic ulcer. It supplies the nutritional requirement, antacid buffering capability, antihemorrhagic factor and the vitamins which act as a tonic on the gastrointestinal tract and on the individual as a whole.

Material and Results

Thirty-three patients representing acute, subacute and chronic stages of benign peptic ulcer all of whom were refractory and failed to respond to previous forms of therapy were selected for this report. The one single common

*Sippyplex Powder®—Supplied through the courtesy of The Purdue Frederick Company.

complaint and manifestation of activity or penetration was pain described with individual variations depending on their sensitivity threshold, such as severe cramps, sharp stitches, heartburn, continuous or intermittent dull ache, indigestion, "gas" or hunger. Seven patients had a history of peptic ulcer dating back from 4 to 30 years. In most of the patients domestic, personal and business tensions were prominent features, one patient had psychiatric therapy, five patients had previous bleeding episodes and one patient had been operated upon for a penetrating ulcer.

All of the patients were studied roentgenographically with results given in Table I and were treated with Sippyplex and modified dietary regimen. The relief obtained in relation to the duration of treatment is outlined in Table II and the over all results in Table III.

Of the four patients who failed to respond to the treatment, one was a female of 48 years with a history of duodenal ulcer for 20 years who had at one

TABLE II

IMPROVEMENT IN RELATION TO DURATION OF TREATMENT

Duration	No. of Patients
1 week	19
2 weeks	4
3 weeks	3
8 weeks	3

time or another been on the whole gamut of antispasmodics, antacids and anticholinergics. Although she was temporarily relieved for a few weeks, the failure to improve suggested a walled off perforated ulcer and she was referred for surgery. The other three patients were characterized by marked psychogenic factors of domestic tensions and worries.

Typical case reports of four patients successfully treated were as follows:

Case 1:—S. G., age 49, single, presented himself with a history of severe epigastric pain beginning six years ago at which time a gastrointestinal x-ray series revealed a duodenal ulcer. The pain continued throughout the six years with little relief in spite of numerous changes in medication. The only relief he obtained followed frequent intake of food, particularly milk.

The present complaints in addition to the severe pain included nausea, vomiting and heartburn, very frequently becoming aggravated during the night, disturbing his sleep and adding to the daily tensions of business activities. An x-ray study (Fig. 1) showed a penetrating duodenal ulcer. He was placed on

Sippyplex powders and began to experience relief beginning after the first week of treatment. His improvement continued during the entire period of observation. A repeat x-ray study three months later (Fig. 2) paralleled the clinical improvement outlining a smooth triangular bulb at the site of the previous ulceration.

Case 2:—R. M., age 51, had enjoyed good health until February 1957, at which time she began to experience "heartburn" not relieved by food or a variety of medications. She had been smoking excessively because of continuous daily tensions. Three months after the onset of her illness, continuous severe

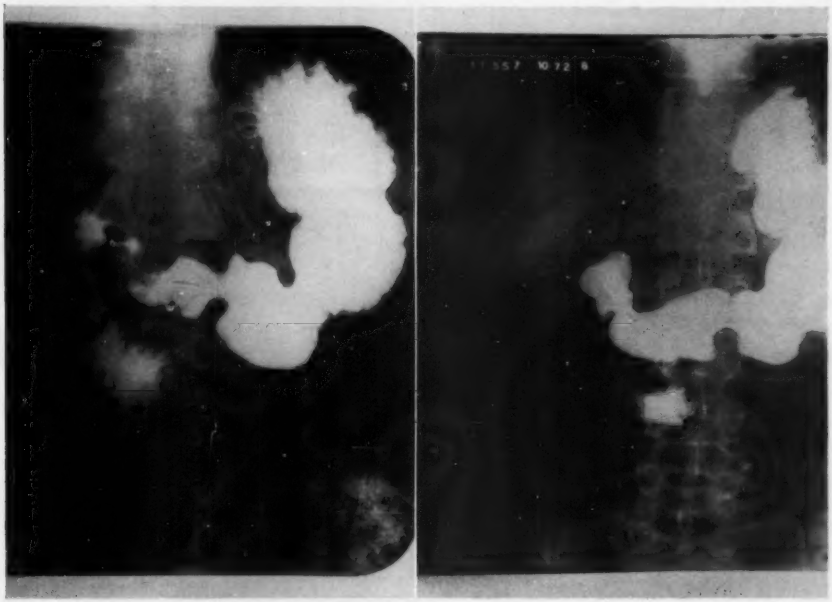

Fig. 7 Fig. 8

blood tinged vomiting began, resulting in an attack of massive hemorrhage and syncope necessitating hospitalization and repeated transfusions.

Recovery proceeded slowly because of anorexia and heartburn. At this stage of her illness she was given a Sipplyplex powder regimen together with an antispasmodic. Improvement began and continued after the first week of treatment at which time the antispasmodic could be discontinued.

X-ray studies (Figs. 3 and 4) taken before and 3½ months after treatment (Figs. 5 and 6) showed complete healing of a large penetrating ulcer on the lesser curvature of the stomach.

Case 3:—Patient, age 64, had been complaining for the past month of daily unrelieved epigastric pains and vomiting occurring one to two hours after meals. The only relief he obtained, particularly during the night, was small frequent milk feedings.

TABLE III

Final Results of Treatment	No. of Patients
a. Asymptomatic	22
b. Improved	7
c. Failures	4

An x-ray study revealed a penetrating duodenal ulcer (Fig. 7). After one week on Sippyplex powders without any dietary restrictions, the nocturnal epigastric pain completely disappeared, and the daytime intensities subsided to about 50 per cent. At the end of the second week and since then except for an

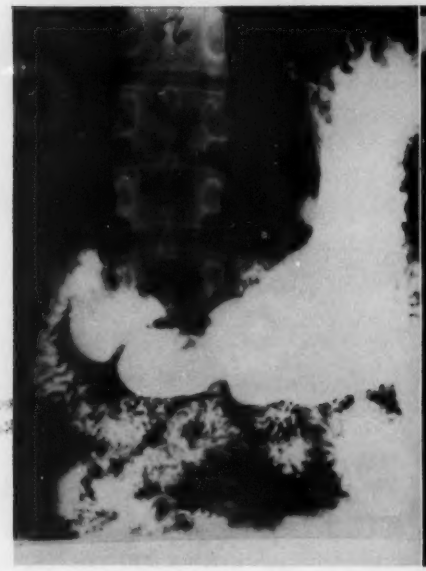

Fig. 9

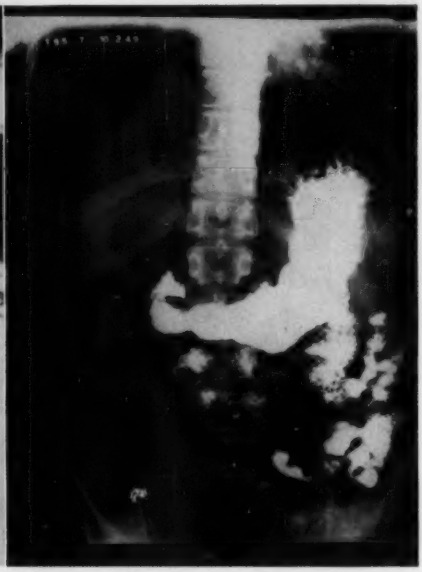

Fig. 10

occasional episode of pain, he has been completely asymptomatic and free from all pain.

Follow-up x-ray (Fig. 8) taken three months later showed absence of the penetrating duodenal ulcer originally present.

Case 4:—Male, age 58 years, presented himself with x-ray's taken on 3 Nov. 1956 (Fig. 9) revealing a large penetrating ulcer on the lesser curvature of the stomach. His complaints consisted of severe epigastric pain and heartburn not responding to a variety of antacid and anticholinergic medication.

A regimen of Sippyplex powders, an antispasmodic and modification of the diet was instituted. He became completely asymptomatic at the end of the first week permitting the discontinuation of the antispasmodic and a return to normal diet. The Sippyplex powders were continued for a period of eight weeks at which time follow-up x-ray (Fig. 10) showed complete healing of the penetrating gastric ulcer.

Comment

Palmer and Heinz[3] observed that ulcer pain is relieved by aspirating the acid chyme from the stomach and conversely the pain could be induced by introducing the acid chyme back into the stomach. They also noted that if this aspirated chyme was introduced into another ulcer patient, pain would follow.

A peptic ulcer diet should therefore emphasize foods which would be not only nutritionally adequate but would also combine with or adsorb the free hydrochloric acid in the gastric juice. This diet should exclude those foods which act as chemical or mechanical irritants thus stimulating excessive gastric secretion and motility. Protein deficiencies are not uncommon among patients with chronic peptic ulcer, but no specific defect in protein metabolism exists which cannot be corrected by an adequate protein intake[4].

The same factors required to increase the resistance of the human body against disease are also required to increase the resistance of the mucous membrane of the stomach and intestine against the acid pepsin combination. If we place our patients on any strict dietary regimen, it must follow that a deficiency will occur. What good can be gained by supplying the necessary calories but depriving the gastrointestinal mucous membrane of vitamins, minerals or protein necessary for rebuilding and regeneration of the affected ulcer areas. If we compare the repair of a damaged house with the repair of a peptic ulcer, it will be noted that any curtailing of the number of bricks, amount of cement, or sand would result in either a poor repair or none at all. In the repair of the ulcer, sufficient proteins, minerals and vitamins must therefore be present to help in the healing and regenerative process.

The site of the ulcer area must be in an environment beneficial to such repair. All inimical factors should be neutralized and reduced to a minimum. Proteins have the property of combining and reducing the hyperchlorhydria. The frequent intake, however, of protein for its antacid effect would be impractical. Therefore the addition of a nonabsorbable alkali to the dehydrated milk is the most effective way of combating the acid pepsin factors. The non-

absorbable alkali not only acts chemically by neutralizing the acid but also acts mechanically by forming "a coat of armor" on the ulcer base thus diminishing the irritation of both the chemical and mechanical factors.

Conclusions

1. The immediate cause of peptic ulceration is action of acid plus pepsin on a susceptible mucosa. Neutralization of free acid plus provision of good nutrition are basic in ulcer therapy.

2. Sippyplex accomplished both of these basic objectives and is therefore a valuable therapeutic agent in the treatment of peptic ulcer.

3. Twenty-nine out of 33 patients who were refractory to conventional ulcer therapy, including anticholinergic drugs, liberal ulcer diet and alkalis, responded favorable to this form of therapy.

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REGIONAL ILEITIS*

Report on Two Cases

BORIS SOKOLOFF, M.D.
CLARENCE C. SAELHOF, M.D.
and
BENJAMIN McCONNELL, M.D.
Lakeland, Fla.

Twenty-five years ago, Crohn et al[1] gave the original description of regional ileitis as a clinical and pathological entity. During these years, much was learned about the clinical course of this disease and the pathologic changes present in it. The cause of this disease, however, still remains unknown (Crohn and Janowitz[2]). No effective treatment, except surgery, is available in this condition.

An attempt was made by us to relieve the manifestations of ileitis by administering citrus bio-flavonoids in two cases of this disease.

Case Histories

One case was that of a girl, 8 years of age, who had an acute form of ileitis. The other treated case was of a man, 65 years of age, with a chronic regional enteritis, of long standing.

Case 1:—H. G., female, 8 years of age, white. No past history of gastrointestinal disorders. On 15 April 1957, complained of acute pain in her abdomen, with a fever of 102°; nausea and vomiting.

Examination:—Lung, heart, throat normal. The symptoms indicated acute appendicitis. On 15 April appendix was removed. It showed no inflammation. The terminal ileum appeared engorged and slightly rigid. A small amount of free peritoneal fluid and a very mild mesenteric adenitis were disclosed.

Diagnosis:—Acute regional ileitis.

Treatment:—The patient was placed on citrus bio-flavonoids (CVP syrup†), two teaspoonfuls, three times a day. The fever subsided on the third day and the abdominal pain gradually disappeared by the sixth day of treatment. The roentgen examination on 10 May 1957 disclosed no pathology of the small intestines, an indication of a complete recovery from the disease.

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*From the Southern Bio-Research Institute, Florida Southern College, Lakeland, Fla.
Presented at the Annual Meeting of the Medical Section, Florida Academy of Sciences, Stetson University, 6 December 1957.
Aided by a grant from the Marcia Tucker Foundation, New York, N. Y.
†CVP, water soluble citrus bio-flavonoid preparation manufactured by U. S. Vitamin Corp., N. Y.

Comment:—In this case of acute ileitis, the patient responded favorably to bio-flavonoid therapy.

Case 2:—A. E., male, age 65, white. Long past history of gastrointestinal disorders. Complained of occasional stomach aches, poor bowel evacuation, incidences of constipation and diarrhea, and abdominal pain. On 12 December 1956 acute abdominal pain, vomiting, weakness and slight fever 100°.

Roentgen findings:—The proximal ileum involved. The loops of bowel markedly separated and rigid. Cast-like appearance of the mucosal pattern. Presence of several inflammatory polyps. Eccentric skip areas.

Diagnosis:—Regional ileitis. No stenosis.

Treatment:—Was placed on citrus bio-flavonoids (CVP) 200 mg. three times a day in capsules. Soft diet. Slight improvement in ten days: decrease in pain, improvement in bowel movement. Continued bio-flavonoid therapy. On 14 January 1957 roentgen findings showed the loops less markedly separated. The mucosal folds still thickened but not fused. The contour of the lumen more regular than before. Continued bio-flavonoid therapy. On 12 March 1957, roentgen findings indicated some thickness of the mucosal folds. The loops were less rigid than before. The inflammatory polyps decreased in size. General condition satisfactory. On 4 November 1957, roentgen findings showed the contour of the lumen still irregular, with a few blunted folds visible. The loops moderately rigid. General condition satisfactory.

Comment:—This is a case of a patient with a mild nonstenotic regional ileitis, who possibly responded favorably to the bio-flavonoid therapy. The disease was not cured but the pathologic lesions became less pronounced as a result of the treatment.

Experimental Premises

In search for the etiologic agent in regional ileitis, much attention was given to finding similar diseases in animals. Recently Emsbo[3] described a disease of the ileum in swine that resembles regional ileitis in its distribution of a necrotizing granulomatous process. No causative agent, however, has been detected in the porcine ileitis. We, in turn, investigated mucous enteritis in rabbits, which affects mostly young animals. The mortality rate from this disease is very high, often reaching 95-100 per cent. So far, the attempts by various investigators (Templeton[4], and others) to produce the disease experimentally have failed. No microbial agent was detected and the disease apparently is not of a bacterial origin. No modern technics were used by other investigators for detecting a viral agent. Our histopathologic studies showed the cells of the submucosal layers to be desquamated and vacuolized. A localized submucosal lymphoidal hyperplasia was evidenced with the formation of a few giant cells. Congestion and alterations of arterioles and capillaries with small hemorrhagic

areas in the submucoidal tissue were suggestive of the presence of the capillary syndrome. The autopsy specimens taken at the early stage of disease and stained by the May-Grunwald-Giemsa technic showed inclusion bodies in the lymphatic cells, indicative of a viral infection. The histopathologic pattern present in the mucous enteritis of rabbits showed a similarity with that described in the regional enteritis in children.

During the years 1956-57, 237 suckling rabbits at the Hamilton Station, Roscoe B. Jackson Laboratory, became affected with acute enteritis. 154 of these rabbits were not treated. Eighty-three rabbits were given, orally, the citrus bio-flavonoid compound, CVP in a syrup form, for 1 to 14 days, two times a day. The results of this therapy indicated beneficial effect of these compounds in acute enteritis of rabbits.

TABLE I*

154 nontreated rabbits, control Mortality rate:	100%
14 received CVP for one or two days Mortality rate:	100%
69 received CVP for 4-14 days Mortality rate:	10.5%

The physiologic premises for treating acute enteritis in rabbits with bio-flavonoids were based on the fact that in this condition, capillary injury and hemorrhage were evidenced in the submucosal layers of the ileum. A number of papers were published about the usefulness of citrus bio-flavonoids in conditions where the capillary syndrome was present, such as gastrointestinal hemorrhage (Weiss et al[5]); erythroblastosis (Rogers and Fleming[6]; Jacobs[7]); retinitis (Loewe[8]; Shepardson and Crawford[9]); habitual abortion (Greenblatt[10]; Javert[11]; Taylor [12]; Pearse and Trisler[13]); the capillary syndrome in viral infections (Sokoloff[14]) and other conditions where capillary injury was apparent.

It was on the basis of this experimental data concerning the therapeutic value of bio-flavonoids in acute enteritis in rabbits, that it was decided to treat the two cases of ileitis with this preparation.

Comment

The etiological agent either in regional enteritis in man or in acute enteritis in rabbits is not known. The English workers (Cooke[15] and others) offered a theory that some local disturbance in fat metabolism, or abnormality in fat

*This part of the experimental study was conducted at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine under the direction of Dr. P. B. Sawin.

absorption might be responsible for the pathologic changes in ileitis. Warren and Sommers[16] seem inclined to adhere to this viewpoint, on the basis of evidence regarding the presence of the products of lipolysis in the lymphatic tissue of the affected ileum. The alterations in fat metabolism were, however, not reported in acute enteritis in children. No abnormal fatty deposits are present in acute enteritis in rabbits. One may feel that the local disturbance in fat metabolism observed in regional ileitis is a secondary phenomenon, the results of some alteration in the physiology of affected lymphatic cells.

Mucoid enteritis in rabbits is an entity not identical with the regional enteritis in man. Yet there is much similarity in the pathologic pattern between this disease and the acute enteritis in children: a prompt recovery from the disease, moderate involvement of the submucosal lymphatic tissue, the presence of a few giant cells, and the engorgement of small blood vessels. The cytologic study revealed the presence of inclusion bodies in the submucosal lymphatic cells in rabbits, typical of some viral invasion. The theory of viral etiology of regional ileitis offered by us, is not inconsistent with the clinical picture in this disease, with the sudden onset of symptoms occurring in some patients of the older age group, and almost always in children. This theory, however, must be proved by further virologic studies in which our group is currently engaged.

Summary

Two clinical cases of regional enteritis, one in an adult and the other in a child, both treated with citrus bio-flavonoids benefited from this therapy.

Mucoid enteritis in rabbits was treated with citrus bio-flavonoids. This treatment reduced the mortality rate from 100 to 10.5 per cent.

Cytologic studies have revealed the presence of inclusion bodies, indicative of a viral invasion in the submucosal lymphatic cells of rabbits affected with acute enteritis.

A virus theory regarding the causative agent of regional enteritis was suggested.

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NEWS NOTES

Mexico Regional Meeting

The Regional Meeting in Mexico City, which has been arranged through the cooperation of Dr. Pedro Ramos and Dr. Aaron Lieberman, will be held at the Auditorium of the Hospital Central, S.C.O.P., in Mexico City on Monday, 27 October 1958.

The program for the day will consist of eight individual papers, five of which will be presented by doctors in Mexico, affiliated with the College. The other three papers are to be presented by doctors from the United States.

There will be a $10.00 registration fee for those attending. The program has been mailed out to the membership of the American College of Gastroenterology and appeared in the September 1958 issue of The American Journal of Gastroenterology.

Postconvention Trip to Mexico

A Postconvention Trip to Mexico has been arranged for those attending the 23rd Annual Convention and Course in Postgraduate Gastroenterology of the American College of Gastroenterology, which is being held in New Orleans, La., 19-25 October 1958.

A low cost ten day trip, starting either on Thursday, 23 October or Sunday, 26 October, is available. Included in the cost will be meals, transportation and hotel accommodations while in Mexico. Those taking the trip will also attend the Mexico Regional Meeting in Mexico City on Monday, 27 October 1958.

Reservations for the trip can be made through World-Wide Travel Service Corporation, 1800 H. Street, N.W., Washington 6, D. C. or by contacting their representative at the Convention in New Orleans.

In Memoriam

We record with profound sorrow the passing of Dr. A. Judson Quimby of New York, N. Y., Associate Fellow of the American College of Gastroenterology. We extend our deepest sympathy to the bereaved family.

One-Day Symposium on Peptic Ulcer

The Louisiana State University of Medicine in New Orleans, in cooperation with the Section on Gastroenterology of the Southern Medical Association, is sponsoring a one-day Symposium on Peptic Ulcer on Saturday, 1 November 1958.

There will be a registration fee of $10.00 for the symposium. Additional information may be obtained from the Chairman and Moderator, Dr. G. Gordon McHardy, 3636 St. Charles Ave., New Orleans 15, La.

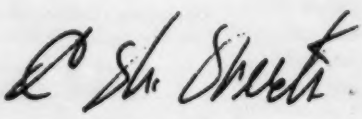
President's Message

A Successful Year

As we near the time for the election of new officers it seems appropriate to review the course of our activities. From the standpoint of membership, finances and administration, I believe our organization is sound. Although such a foundation is of the utmost importance in any organization, its major significance to me, is that it offers the opportunity whereby the objectives of the society can be achieved.

To me, our objectives, as I mentioned on this page about a year ago, consist of holding annual scientific meetings, providing postgraduate courses and the publishing of a journal of high quality as a means of extending and disseminating our knowledge in the field of gastroenterology.

As we gather in New Orleans for the 23rd Annual Convention on 19 October 1958, I feel sure each member of the College will find tangible proof of the efforts that have been put forth to meet these objectives.



ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

CONGENITAL TRACHEOESOPHAGEAL FISTULA WITHOUT ATRESIA OF THE ESOPHAGUS: Benjamin P. Clark and J. O. Morgan. J.M.A. Alabama 27:83 (Oct.), 1957.

The authors report a fairly classical picture of tracheoesophageal fistula without atresia of the esophagus. Despite careful studies, it took more than four months to demonstrate the presence of the lesion. Careful and repeated x-ray and endoscopic examinations were required. The esophageal opening could not be found at surgery after the fistula had pulled loose from the trachea. However the child made an uneventful recovery.

JOHN M. MCMAHON

STOMACH

UPPER GASTROINTESTINAL BLEEDING IN THE AGED: Wayne H. Thompson and James M. Leffel. Indiana M. A. 50:1337 (Oct.), 1957.

Analysis of hospital records was made in regard to a group of patients over 60 years of age presenting gastrointestinal bleeding problems. A total of 248 cases was reviewed with approximately 142 consecutive cases being from a large private hospital in the years 1954 and 1956 and a comparable number from a large charitable hospital in the years 1951 to 1956. Careful observation and medical consultation were recommended and in most cases surgery should be done within the first 48 hours if feasibly possible. In this particular series surgery for peptic ulcer was accomplished with 2 per cent mortality. There were an additional 36 cases with massive hemorrhage in which a mortality of 27.8 per cent was noted. Of those dying of gastrointestinal bleeding 73 per cent were patients over 60 years of age. Operation of choice recommended was that of subtotal resection but in rare instances a lesser procedure such as ligation of the ulcer with exclusion of the ulcer by wedge resection may be life-saving in a patient who is in a critical status. The cases in which the source of bleeding was not determined, a high subtotal gastric resection was completed. The point was again emphasized that gastrointestinal hemorrhage of the

aged is a very serious disease associated with high mortality which requires the utmost care and surgical skill in medical management. In this particular series the most common sources of bleeding were found to be esophageal varices, gastric ulcer and duodenal ulcer in that order.

JOSEPH E. WALTHER

HAZARDS IN THE MANAGEMENT OF PEPTIC ULCER WITH ANTICHOLINERGIC DRUGS. A RE-EMPHASIS AND RE-EVALUATION: Hyman J. Roberts. J. Florida M. A. (Oct.), 1957.

The author emphasizes several infrequently considered complications of anticholinergic drug therapy in peptic ulcer that should be kept in mind prior to its administration on a routine basis. These consist of complete pyloroduodenal obstruction, ileus, and unrecognized ulcer activity leading to subsequent perforation. This consideration is all the more important if a chronic partial obstruction has not been specifically excluded. Ileus can also ensue on such therapy in the presence of massive gastrointestinal bleeding due to causes other than ulcer. The use of these drugs is advised with caution in the presence of heart failure or coronary insufficiency because of tachycardia and myocardial ischemia which may be induced. They may also precipitate glaucoma and urinary retention.

BERNARD STERN

DIGESTIVE AND METABOLIC DISTURBANCES AFTER TOTAL GASTRECTOMY. RESULTS OF VARIOUS METHODS OF RE-ESTABLISHING DIGESTIVE CONTINUITY: J. Govaerts, M. Colard, R. Keikens and J. Van Geertruyden. Arch. mal. app. dig. 46:109 (27 Oct.), 1957.

Total gastrectomy brings in its wake a series of digestive and metabolic disorders which make up the syndrome of agastria. The pathogenesis of these disorders is studied. Various corrective operations have been proposed and are reviewed here. A comparative study of cases which have been published and also of private cases enables one to judge the functional results of each type of operation. These results are most favorable when duodenal passage is re-established (homogeneous mixture of food with pancreatic and biliary juices, more complete absorption of fats and proteins) and when an intestinal loop is interposed in isoperistaltism between the esophagus and the duodenum (disappearance of dysphagia, increased alimentary capacity). Among the different methods suggested, the best seems to be the one involving jejunal interposition.

GUY ALBOT

GASTRECTOMY WITH JEJUNAL REPLACEMENT: Austin Henley. Arch. mal app. dig. 46:95-109 (27 Oct.), 1957.

The author gives an account of the study, over a 5-year period, of 115 patients on whom a gastrectomy with jejunal replacement was performed.

He does not recommend this operation for patients with duodenal ulcer. After total gastrectomy, the jejunal reconstruction of the gastric reservoir seems to him an effective method.

GUY ALBOT

PHYSIORADIOLOGY OF GASTRECTOMISED PATIENTS WITH PRESERVATION OR RE-ESTABLISHMENT OF THE DUODENAL CHANNEL: P. Porcher and P. Buffard. Arch. mal. app. dig., 46:155 (27 Oct.), 1957.

If it is to be conceded that some value be attached to the findings of correctly administered radiological tests – barium, then the meal–recorded at each important juncture, the timing of total evacuation is by itself too summary, and radiocinema is necessary for a worthwhile study. It is clear that the preservation or the re-establishment of the duodenal channel produces the appearance and above all the behavior near-

est to anatomical and functional completeness.

On the other hand, if the problem is considered from the radiological point of view, everything takes place as if this type of operation needed in particular, both in the pre- or postoperative indication and in the quality of the surgical act itself, mature reflection, long experience and a great mastery of technic.

GUY ALBOT

A COMPARISON OF THE VALUE OF VARIOUS GASTRECTOMY TECHNICS: Georges Lagache and Emile Delannoy. Arch. mal app. dig. 46:5-25 (27 Oct.), 1957.

From statistics of 538 cases of gastrectomy, the authors study the respective advantages of gastrojejunal and gastroduodenal anastomoses. Three hundred seventy-seven Finsterers and 161 Peans were analyzed in terms of the different factors which cause a gastrectomy to be or not to be well tolerated.

They also make a comparative study of gastrectomies carried out for gastric ulcer and for duodenal ulcer and a distinction is made between operations carried out in hospital and those performed on private patients by the same surgeon.

Apart from a more constant ponderal recovery, the advantages of the Pean over the Finsterer appear relatively slight.

GUY ALBOT

INTESTINES

ANTIBIOTIC TREATMENT IN DYSENTERY: Ross Johnson and Joan B. Landsman. Scottish M. J. 2:383 (Oct.), 1957.

The authors studied 479 cases of dysentery caused by Sonne and Flexner infections. Sixty-four per cent of these cases were in children less than five years of age.

The following drugs were used in their study namely: Chlortetracycline, Chloramphenicol, Oxytetracycline, Polymyxin B, Neomycin and Sulfadiazine, Streptomycin and Sulfadiazine.

The authors found that a bacteriological cure was obtainable in 96 per cent of cases. Only two of the above drugs, Chlortetracycline and Oxytetracycline, proved to be the most effective. Oxytetracycline was favored because it produced less undesirable side-effects.

ZACH R. MORGAN

CONGENITAL AGANGLIONIC MEGACOLON: H. Gray Carter. Texas J. Med. 53:771 (Oct.), 1957.

The author discusses the definition and diagnosis of congenital aganglionic megacolon. The disease is classified into three types: the short segment, the long segment and the rare central segment type. In discussing the diagnosis, biopsy of the internal sphincter muscle is recommended in addition to x-ray examination. Complications of nonsurgical treatment including water intoxication, ulceration of the colon and frequent severe gastroenteritis are mentioned. Certain features of the technic of the endoanal anastomosis are discussed.

BERNARD FARFEL

POLYPS AND CARCINOMA OF THE COLON: M. B. Goldgraber and J. B. Kirsner. A.M.A. Arch. Int. Med. 100:669 (Oct.), 1957.

There is no direct evidence of malignant transformation of an adenomatous polyp into a carcinoma. The circumstantial evidence is based upon 1. closed parallelism of location, of age and sex distribution, 2. association of polyps and cancer, 3. familial polyposis developing invariably cancers. Colonic cancer is rare in children, however a few cases of cancer with polyps have been recorded in this age group. The causative relationship between inflammatory pseudopolyp and cancer is still more difficult to obtain. (Snapper suggests that familial adenomatosis is the precursor of

both ulcerative colitis and multiple cancers in such cases). The small size of a polyp is no guarantee against malignancy as 3 mm. excrescences may turn out to be cancers. The differentiation between adenoma and papilloma does not help in the prediction of malignant potentialities.

H. B. EISENSTADT

MECKEL'S DIVERTICULUM: Ted Lace. Texas J. Med. 53:785 (Oct.), 1957.

Three cases are reported to demonstrate three common complications of Meckel's diverticulum. The first case, a 4-month old boy, illustrates the finding of gastric mucosa with peptic ulceration and hemorrhage. The second case, a 9-year old girl, was admitted with history of vomiting and abdominal pain. This case illustrated the initiation of intestinal intussusception by the Meckel's diverticulum. The third patient, a 29-year old male, had a 12-hour history of acute abdominal epigastric pain. The patient was operated upon the following day and found to have extensive gangrene of the bowel due to intestinal obstruction. The Meckel's diverticulum, with an attachment at the umbilicus, formed one point of two areas of obstruction.

The embryology and anatomy of Meckel's diverticulum are briefly discussed.

BERNARD FARFEL

MEGALOBLASTIC ANEMIA ASSOCIATED WITH DIVERTICULA OF THE SMALL BOWEL: Stuart R. Townsend and Douglas G. Cameron. Am. J. Med. 28:668 (Oct.), 1957

Three patients are reported with macrocytic anemia, megaloblastic bone marrow and low serum Vitamin B_{12} level. These changes were believed to be caused by stasis in the multiple small bowel diverticula found at x-ray examination. Two of these patients also had gastric achlorhydria, the third had free hydrochloric acid. Other findings were glossitis, steatorrhea, prothrombin deficiency, and undernutrition. Hematological response to Vitamin B_{12} injections was satisfactory. The authors referred to a similar case of multiple small bowel diverticulosis with megaloblastic anemia and sprue manifestations previously reported in the English literature. They consider this as a specific entity related to symptomatic sprue associated with short-circuits and blind loops. However, no studies with radioeobaltamin were performed in these patients.

H. B. EISENSTADT

INTUSSUSCEPTION—OPERATIVE VERSUS NONOPERATIVE TREATMENT: J. W. Duckett. Texas J. Med. 53:761 (Oct.), 1957.

Attention is called to the reduction of mortality in recent years. Earlier diagnosis as well as improvements in medical and surgical care are credited with the lowering of operative mortality. Sixty-seven cases are reported with 7 fatalities pointing out the danger in delay in diagnosis or initiating treatment. The author agrees with previous statements by Ravitch that early treatment with barium enema reduction can be attempted, but should be done in the hospital with all necessary precautions for surgery to follow if decided upon by the attending surgeon. Barium enema reduction is not advised when the symptoms have persisted longer than 24 hours. This time limit may vary in each direction depending on the individual case. The usual supportive measures should be kept in mind at all times.

BERNARD FARFEL

LIVER AND BILIARY TRACT

GALLBLADDER POLYPS: Donald D. Kozoll and Karl A. Meyer. Quart. Bull. Northwestern Univ. M. School 31:225 (Fall), 1957.

Willrock, in 1934, reviewed the literature and found 69 adenomatous polyps in a series of 9,550 cholecystectomies, however, during 1940, Walters and Snell claimed

that 8 per cent of all gallbladders removed had papillomatous polyps!

Both these lesions may be precancerous formations caused by irritative cholesterol concentration on components of the gallbladder mucosa in a progressive train of hyperplasia following a pattern that may be outlined as: 1. proliferation of an Aschoff gland, resulting in an inflammatory polyp, having a flat base, 2. adenomatoid hyperplasia of superficial epithelium within a cholestrol filled stroma, (Cholestroloma) and 3. marked glandular hyperplasia leading to stalk formation with resulting papilloma.

J. EDWARD BROWN

AGRANULOCYTOSIS ASSOCIATED WITH INFECTIVE HEPATITIS: F. E. Dische and J. R. Golding. Brit. M. J. 5047:738 (28 Sept.), 1957.

Virus hepatitis in its early stages depresses the leucocyte count, affecting both the neutrophils and the lymphocytes, but after about two weeks the count returns to normal.

A case is presented where this picture did not obtain.

Necropsy report pointed to virus hepatitis with slightly enlarged liver, wrinkled surface, some areas of necrosis showing through the capsule, sections having broadened portal tracts, but without nodular hyperplasia. The liver cells were large and had fatty degeneration present.

The case is presented with two hypotheses: 1. Virus hepatitis producing agranulocytosis with secondary infection following, or 2. Secondary infection compounding an already depressed bone marrow resulting in agranulocytosis.

J. EDWARD BROWN

INFECTIOUS HEPATITIS: REPORT OF AN OUTBREAK PROBABLY CAUSED BY DRINKING WATER: James W. Mosley and W. W. Smither. New England J. Med. 257:590 (26 Sept.), 1957.

Eighteen cases of infectious hepatitis in Daviess County, Kentucky were investigated and the epidemiologic evidence concerning transmission is presented. It was thought that at least nine of the cases were due to drinking water from private wells contaminated from the first known case. Positive contamination of the water supply from a septic tank was concluded after dye was placed in the toilet on three occasions and water samples collected from various wells. At all houses tested, dye appeared in the wells after variable intervals. It is concluded that water-borne hepatitis may be more frequent than is reported, particularly in rural areas where water supplies are often unprotected.

JOHN E. COX

SECONDARY HEMOCHROMATOSIS IN ALCOHOLIC SUBJECTS: THEORETICAL PROBLEMS AND CLINICAL DIAGNOSIS: M. Cachin, F. Pergola, R. Levillain, R. Leluc and B. DeBesse. La Semaine des Hopitaux de Paris 33:3174 (Sept.), 1957.

With special reference to 7 personal cases the authors review the literature and give a general study of secondary hemochromatosis in alcoholic subjects. Its incidence does not seem very high when it was systematically fetched in the course of alcoholic cirrhosis with particular care for its being distinguished from mere hepatic cytosiderosis. It should be placed very near those deficiency hemochromatoses which are nowadays well known on both clinical and experimental grounds. That is the way its physiopathology should be considered, although not quite elucidated yet.

The authors emphasize the criteria that should be required for affirming the diagnosis of "fruste" or latent hemochromatosis: anatomical criteria demonstrative that the pigmentary overload is not confined to the liver (the use of gastrobiopsy proving here to be an indispensable technic); biological criteria bringing evidence of iron metabolism disturbances (assessment of the plasma iron having to be perfected with the induced hypersideremia test and with the determination of the fixation potency of the iron *in vitro*). Attention should be called to the concordance of such tests as parallelly positive in true hematocromatosis and parallelly negative in the case of simple cytosiderosis.

DELTA-CORTISONE AND ASCITIC CIRRHOSES: M. Cachin, F. Pergola, F. Potet, R. Levillain and R. Leluc. La Semaine des Hopitaux de Paris 33:3168 (Sept.), 1957.

Sixty cases of ascitic cirrhoses were treated with delta-cortisone in an average dosage of 30 mg. daily, duration of the treatment varying from 20 days to 3 months. In 27 cases (45 per cent) a drying-up of the ascites and edema was obtained. In 6 very severe cases the immediate evolution appeared to be thoroughly transformed by the hormonal therapy.

Yet the long-term prognosis was not so favorable when there was resumption of alcohol addiction. Of 21 subjects, seen after about 15 months, only 11 were in a good condition and 5 were dead.

The side-effects of the drug were of digestive order; 6 cases of hematemesis were observed in the course of treatment, but only in 2 cases was the hematemesis likely to be caused by the hormotherapy. Such ulcerations of the stomach as shown on postmortem were probably due to delta-cortisone, but not unquestionably so.

THE PART OF HEPATIC INVOLVEMENT IN THE NERVOUS COMPLICATIONS OF ALCOHOLISM: F. Pergola and M. Cachin. La Semaine des Hopitaux de Paris 33:3161 (Sept.), 1957.

A clinical, biological and histologic study of the liver was carried out in 117 alcoholic subjects, of whom 31 were showing discrete mental disorders, 45 a typical D.T., 39 a polyneuritis and 2 a Gayet-Wernicke encephalopathy.

This study demonstrated the frequency of histological alterations of the liver in nervous complications from alcoholism. Steatosis was commonly observed and very often combined with sclerosis, especially in the case of polyneuritis. There was even a high incidence of true cirrhosis in a number of cases.

Such lesions were often shown to be clinically and biologically latent. No obvious correlation was to be noted between the severity of the histological changes of the liver and the severity of the nervous complications, so that the role of the hepatic anatomical changes in the development of the nervous accidents seemed to be of moderate significance.

CHOLECYSTECTOMY FOLLOWED BY ASCITES, FEVER AND OLIGURIA: Clinicopathologic Conference. Am. J. Med. 23:481 (Sept.), 1957.

A 51-year old housewife had elective surgery for cholelithiasis. Postoperatively she went into shock, the abdomen had to be reopened to ligate the bleeding cystic artery stump. Hereafter, she was in a stage of septicemia and toxemia with fever, oliguria and a large amount of straw-colored ascites. Death occurred six weeks postoperatively. Autopsy revealed a saculated bile peritonitis restricted to the lesser sac as well as to a walled-off compartment of the main peritoneal cavity as the cause of the postoperative sickness. This bile accumulation was produced by a transected right hepatic bile duct. The bile peritonitis was responsible for a toxic nephrosis as well as for the large serous fluid accumulation in the main peritoneal space.

H. B. EISENSTADT

PANCREAS

STUDIES ON URINARY LIPASE: Martin M. Nothman, Joseph H. Pratt, Allen D. Callow. A.M.A. Arch. Int. Med. 100:221-227, 1957.

Elevation of urinary lipase occurs in practically all cases of acute and most of chronic pancreatitis, just as an increase of serum and urinary amylase. However, these enzymes are not elevated at the same time, and in the same degree. Urinary lipase is also elevated in diseases of organs adjacent to the pancreas, for instance, in cholecystitis and cholelithiasis, cancer of the biliary tract and of the stomach and of the papilla

of Vater, in cirrhosis of the liver, retroperitoneal tumors, penetrating and perforating ulcer, and during renal insufficiency. In contrast to these abnormal findings all patients with cancer of the pancreas have normal lipase figures; however, after secretin stimulation they do not show the increase of lipase excretion seen in normal persons as well as in the previously mentioned pathological conditions.

H. B. EISENSTADT

LACTESCENCE OF SERUM FOLLOWING EPISODES OF ACUTE ALCOHOLISM AND ITS PROBABLE RELATIONSHIP TO ACUTE PANCREATITIS: Margaret J. Albrink and Gerald Klatskin. Am. J. Med. 23:59 (July), 1957.

Five chronic alcoholics showed marked lactescence of their serum due to an increase of all lipid components following a bout of drinking. All experienced sudden abdominal pain at the time of their hyperlipemia which was either diffuse or periumbilical. This was attributed to an acute pancreatitis. Serum amylase remained normal in all cases. Nevertheless, that would not exclude acute pancreatic disturbance. One patient was subjected to exploratory laparotomy where acute pancreatitis was found. The various mechanisms that could give rise to fatty serum during acute pancreatitis are discussed. There might be a suppression of lipocaic, an interference with absorption of unsaturated fatty acids, a decrease of fat-binding serum albumin, a change of the normal calcium fatty acid relationship. In addition, liquefied fat necrosis might have gained access to the blood circulation.

H. B. EISENSTADT

PATHOLOGY AND LABORATORY RESEARCH

COMPARATIVE VALUE OF SERUM AND URINARY AMYLASE IN THE DIAGNOSIS OF ACUTE PANCREATITIS: Eugene I. Saxon, William C. Hinkley, William C. Vogel and Leslie Zieve. A.M.A. Arch. Int. Med. 90:607, 1957.

Urinary amylase is a valuable test for the diagnosis of pancreatic diseases if the total excretion per hour and not only the concentration of an at random specimen is determined. Normal hourly excretion is up to 300 units, 24-hour excretion up to 4,000 units of amylase. As this enzyme is rapidly excreted its increments in the urine during disease are much higher than the corresponding serum level changes. In addition, urinary amylase elevation persists for a much longer time than that in the serum. Only in the presence of renal insufficiency is this test useless, however, under such conditions the serum amylase is also misleading. Twenty-one patients are reported with pancreatic diseases showing normal serum and increased urinary amylase. The latter test did not only confirm the diagnosis of acute pancreatitis but also showed abnormal pancreatic function in a case of leptosporosis with severe abdominal pain and in another case with chronic pancreatic cyst. It also revealed the untoward effect of surgical procedures, x-ray manipulations and early feeding in cases of acute pancreatitis as the urinary amylase values rose immediately after such procedures, which must therefore be considered hazardous.

H. B. EISENSTADT

RESEARCH ON FATTY LIVER. V. ON FATTY LIVER INDUCED BY ETHIONINE: Hiroshi Okuzono, Sho Watanabe, Hisao Serikawa and Nobuhide Nakano. Kumamoto M. J. 10:1 (31 Mar.), 1957.

The authors set out to examine the influence of anthranilic acid, 3-hydroxy anthranilic acid, 5-hydroxy anthranilic acid and chloropromazine on the power of ethionine in producing fatty liver.

From the results obtained on the influence of anthranilic acid, 3-hydroxy anthranilic acid, 5-hydroxy anthranilic acid, chloropromazine, and splenectomy on the effect of ethionine to produce fatty liver, the following conclusions were drawn:

1. Anthranilic acid, 3-hydroxy anthranilic

acid, 5-hydroxy anthranilic acid and chloropromazine were not able to prevent the occurrence of fatty liver induced by ethionine. 2. Splenectomy was not able to inhibit the occurrence of the fatty liver induced by ethionine.

JACOB A. RIESE

THE INFLUENCE OF ASCORBIC ACID UPON THE LIVER: G. C. Willis. Canad. M. A. J. 76:1044 (15 June), 1957.

The author describes the changes which occur in the livers of guinea pigs as a result of deprivation of ascorbic acid.

He reaches the following conclusions: Scurvy manifests itself in the liver by fatty degeneration, acute nonfatty hepatocellular degenerations, massive necrosis and changes in the hepatic reticulin. None of these lesions are prevented by cystine or choline or a combination of them. Some of these are reversible with ascorbic acid replacement.

SAMUEL L. IMMERMAN

STOMACH CANCER AND ABO BLOOD GROUPS: Mitsuo Segi, Susumu Fujisaku, Minoru Kurihara and Hidetaka Moniwa. Tohoku J. Exper. Med. 66:42 (25 June), 1957.

The corelationship between cancer and the ABO blood groups has again come to the attention of medical science.

The authors have made a comparative study of the distribution of blood groups of stomach cancer patients with that of the general population in Japan. In 1,385 cancer cases blood group A was found in 41.2 per cent, B in 21.4 per cent, O in 29.7 per cent and AB in 7.7 per cent.

In comparison with blood group distribution in the general Japanese population, they found the percentage of A group was significantly larger, and that of AB group was significantly smaller among cancer patients than among the general population.

LOUIS K. MORGANSTEIN

FURTHER OBSERVATIONS ON PATIENTS WITH MALIGNANT CARCINOID: Albert Sjoerdsma, Herbert Weissbach, Luther L. Terry and Sidney Udenfriend. Am. J. Med. 23:5 (July), 1957.

The authors present studies on 19 patients with metastatic carcinoid. It is now clear that there is a variability of clinical manifestations associated with carcinoid. Some patients with extensive metastatic carcinoid do not show all, or even the predominant manifestations of the "carcinoid syndrome". Chemical analyses confirm previous findings of excess serotonin production in this disorder. Also, the findings of low fasting plasma tryptophan and urinary N'-methylnicotinamide in some patients substantiate previous suggestions of a disorder in tryptophan metabolism in this condition. A tracer study, in one patient, with the serotonin precursor, 5-hydroxytryptophan, enabled calculation of the tumor pool of serotonin (2,800 mg.), its turnover rate (one-half life of five and one-half days), and the tumor mass (between 1 and 3 kg.). Increases in the urinary excretion of 5-hydroxyindoleacetic acid (5HIAA) in a patient during severe flushing episodes suggests that the flushes are mediated by increased serotonin release even though no concomitant rise in blood serotonin could be measured. Cardiac catheterization studies revealed no measurable differences in the serotonin content of mixed venous and arterial blood which, if present, might account for predominant right-heart involvement. Serotonin probably does not penetrate readily into the central nervous system. With the possible exception of chlorpromazine, drug therapy has proved ineffective.

JOHN M. MCMAHON

SODIUM DIURESIS FROM AMPHENONE GIVEN TO PATIENTS WITH CIRRHOSIS AND ASCITES: Stanley J. Wolfe, Bernhard Fast, James M. Stormont and Charles S. Davidson. New England J. Med. 257:215 (1 Aug.), 1957.

The fluid accumulation in the abdomen associated with hepatic disease is partly due to an excessive adrenocortical function, especially to secondary hyperaldosteronism. Therefore, amphenone, an antagonist to these hormones, was administered to two patients with hepatic cirrhosis. It produced diuresis and natriuresis and decreased the ascites formation. Unfortunately, amphenone was too toxic for prolonged use. Apart from gastrointestinal disturbances and skin rashes it caused a hepatic dysfunction resembling hepatic coma with somnolence, flapping tremor, slurred speech, and confusion.

H. B. Eisenstadt

EFFECT OF L-GLUTAMIC ACID ON METABOLISM OF PATIENTS WITH HEPATIC ENCEPHALOPATHY: Joseph F. Fazekas, Howard D. Ticktin, James G. Shea. Am. J. M. Sc. 234:145-149 (Aug.), 1957.

This report is based on the effects of administration of L-glutamic acid on cerebral consumption, blood ammonia levels and electroencephalograms in the presence of cerebral dysfunction due to hepatic insufficiency. Cerebral findings on three patients who recovered spontaneously from hepatic encephalopathy are reported. It was found that administration had a temporary effect in reducing elevated blood ammonia levels. There was no apparent change in clinical condition, cerebral oxygen consumption or electroencephalograms. If the drug was continued the blood ammonia levels returned to the previous high and continued to rise. The authors suggest that exogenous sodium glutamate may saturate or exhaust an impaired glutamine synthesis mechanism.

Bernard Farfel

STANDARD SUGAR LOADING TEST: Yoshio Goto, Kogo Seino and Isao Ito. Tohoku J. Exper. Med. 66:115 (25 Aug.), 1957.

Their criteria for a normal sugar loading test are: a fasting blood sugar below 120 mg. per cent, a peak level below 200 mg. per cent, a 2-hour level below 120 mg. per cent for capillary blood and a negative urine sugar. In diabetics evaluation of the loading curve may indicate whether insulin is needed in the treatment schedule. If the fasting blood sugar is below 195 mg. per cent, the 2-hour value below 280 mg. per cent, his diabetes can be controlled by diet alone; if the fasting blood sugar is above 218 mg. per cent, insulin must be used in addition to diet.

However, in their series of nondiabetic patients, they found peaks above 200 mg. per cent in older people; in a case of diabetes insipidus and in one case of gastroenterostomy with no urinary glucose. In this same group in 8 cases of the 36, they found 2-hour values above 120 mg. per cent, which included 2 cases of pancreatic cancer, one case each of lung cancer, cholelithiasis and myelocytic leukemia, 3 cases of strumitis. They emphasize that repeated studies and further evaluation are necessary in equivocal situations.

In the renal glycosuric patient, according to the authors, the loading curve has a peak value of below 200 mg. per cent and a 2-hour value below 120 mg. per cent. If the figures are above these, they are to be considered a mild or latent diabetic.

Saul A. Schwartz

BOOK REVIEWS FOR GASTROENTEROLOGISTS

1956-1957 YEAR BOOK OF ENDOCRINOLOGY: Gilbert S. Gordan, M.D., Ph.D., F.A.C.P., Associate Professor of Medicine, Chief of Endocrine Clinics, Department of Medicine, University of California School of Medicine, etc., etc. 377 pages, illustrated. Year Book Publishers, Inc., Chicago, Ill., 1957. Price $6.75.

Another volume of the practical medicine year books which have become a tradition in medicine. In endocrinology as in the other year books, the editor, with the abstract staff, culls the world's medical literature and abstracts the important items dealing with this subject.

The reviewer, glancing through the table of contents on pages 3 and 4, finds article after article dealing with the various glands, including the pituitary, thyroid, parathyroid, and adrenals. There is also a discussion of the reproductive system and carbohydrate metabolism; evaluation of the sulfonylureic agents, their use and danger in the treatment of diabetes; glucagon and the pancreatic alpha cell.

In fact, the reviewer recommends that the entire section dealing with insulin, etc., should be read by the physician, who undoubtedly will find many useful hints which may be of value to him.

DRUGS—THEIR NATURE, ACTION AND USE: Harry Beckman, M.D., Director, Departments of Pharmacology, Marquette University Schools of Medicine and Dentistry; Consulting Physician, Milwaukee County General Hospital and Columbus Hospital. 728 pages, 126 figures. W. B. Saunders Company, Philadelphia, Pa., 1958. Price $15.00.

In the preface, the author states, "This is a textbook for the undergraduate medical student". This statement is rather underestimated, because the book is a valuable asset to all medical, dental and pharmacy students, as well as physicians who wish to review and relearn the application of drugs in their everyday practice.

Chapter 76 deals with the pharmacology of diagnosis and the drugs used as diagnostic aids, and gives the general practitioner as well as the specialist a comprehensive description of the technic and results obtained with the newer drugs and their interpretation in diagnosis.

An adequate reference at the end of the chapters and a cross index complete the well printed, well bound volume.

Dr. Beckman and the publishers are to be commended for bringing out this useful text.

A MANUAL OF PHARMACOLOGY AND ITS APPLICATION TO THERAPEUTICS AND TOXICOLOGY: Torald Sollmann, M.D., Professor Emeritus of Pharmacology and Materia Medica, School of Medicine, Western Reserve University, Cleveland, Ohio. Eighth Edition. 1535 pages, appendix of bibliography of papers appearing since January 1940 and an extensive cross index. W. B. Saunders Company, Philadelphia, Pa., 1957. Price $20.00.

The eighth edition of Sollman's "Manual of Pharmacology" is more than the title indicates. It is a complete exposé of drugs, their use and application in the realm of medicine. Looking over the contents, the reviewer is impressed with the amount of detail which has gone into this volume to make it the most comprehensive reference for medical students and physicians.

Beginning on page 777, antibiotic substances, indications, side-effects, etc., are elucidated in detail. On page 1285, rare earth metals including Radio-Yttrinn (1288) which is carciogenic, are described. The various mercurial preparations, their application in medicine, makes interesting reading.

The reviewer suggests that medical, pharmaceutical, dental students and all physicians and pharmacists should be owners of Sollmann's "Manual of Pharmacology".

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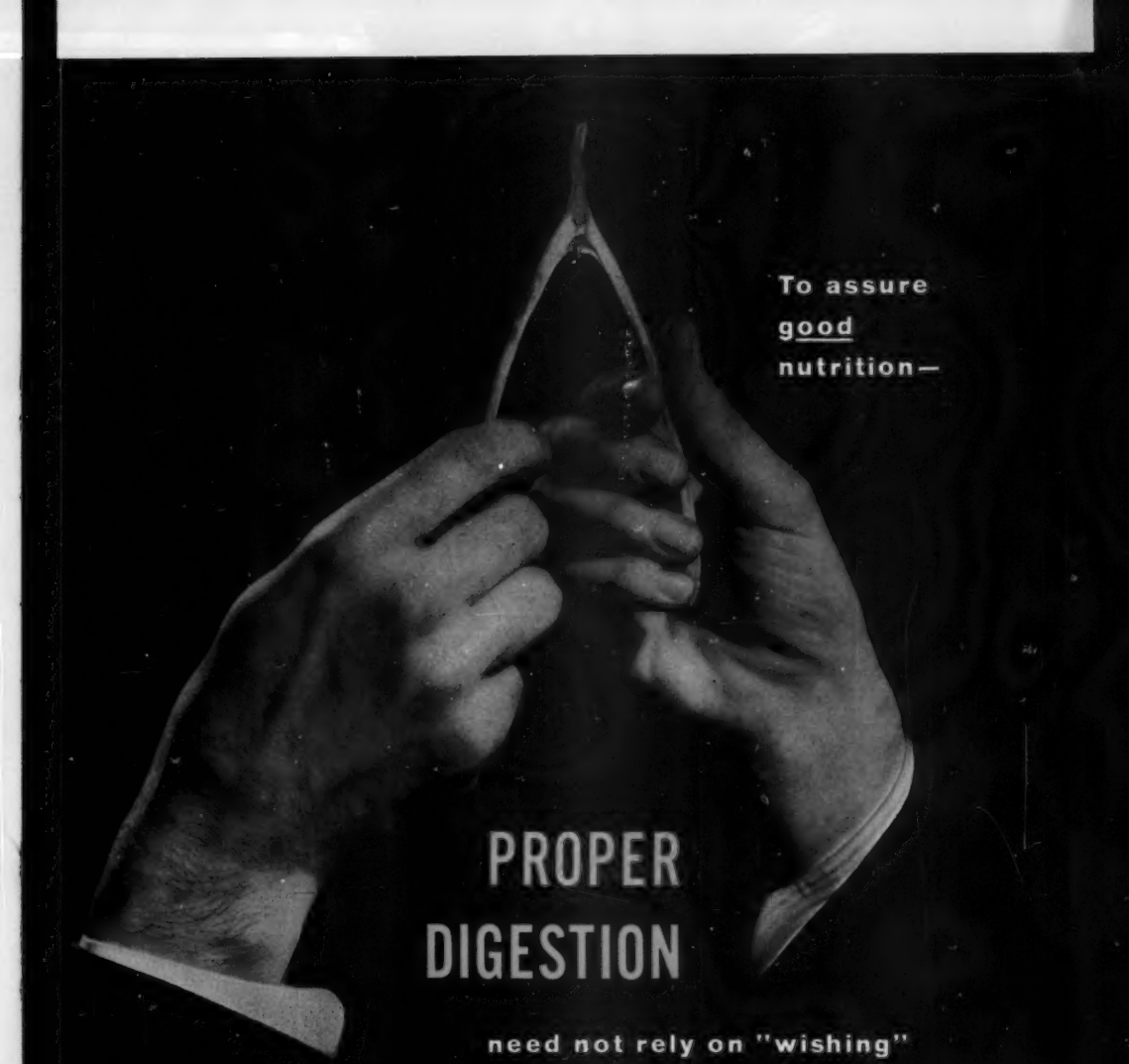

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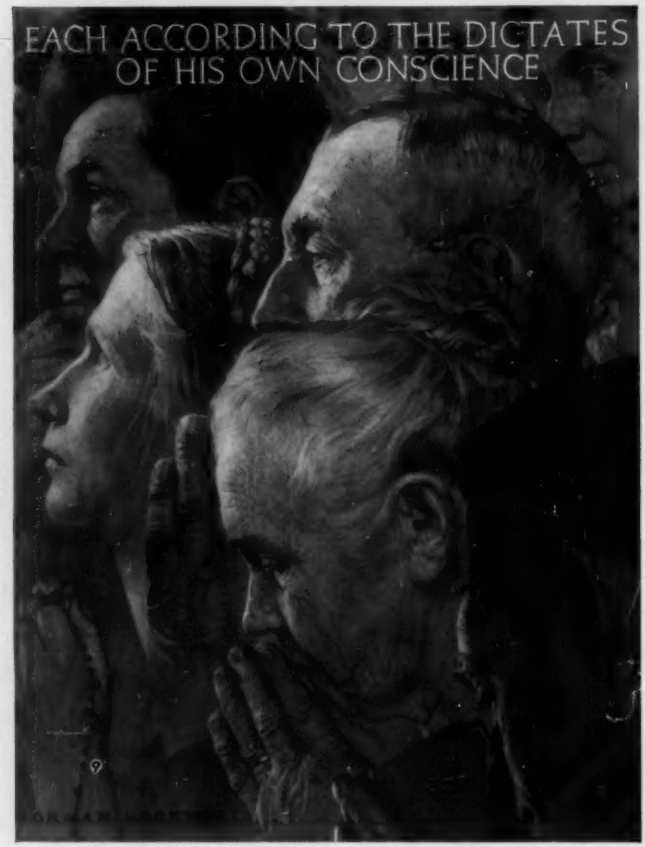

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New GRADUMET TRAL, 50 mg., and GRADUMET TRAL, 50 mg. with Phenobarbital, 30 mg., are supplied at all pharmacies in bottles of 50 and 500. Filmtab TRAL, 25 mg., and Filmtab TRAL, 25 mg. with Phenobarbital, 15 mg., are supplied in bottles of 100 and 1,000. Complete literature, and samples, are available from your Abbott representative

Abbott

®GRADUMET LONG-RELEASE FORM, ABBOTT; PATENT APPLIED FOR
®FILMTAB FILM-SEALED TABLETS, ABBOTT; PATENT APPLIED FOR 808149

throughout the practice of medicine . . .

anxiety

either alone or complicating physical illness

General Practice — Pediatric Psychiatry — Metabolic Disorders

The Neuroses — Neurology — Neuromuscular Disorders

General Surgery — Gastroenterology — Ob. & Gyn.

Cardiology — Dermatology — Allergy

Equanil®

Wyeth

Philadelphia 1, Pa.

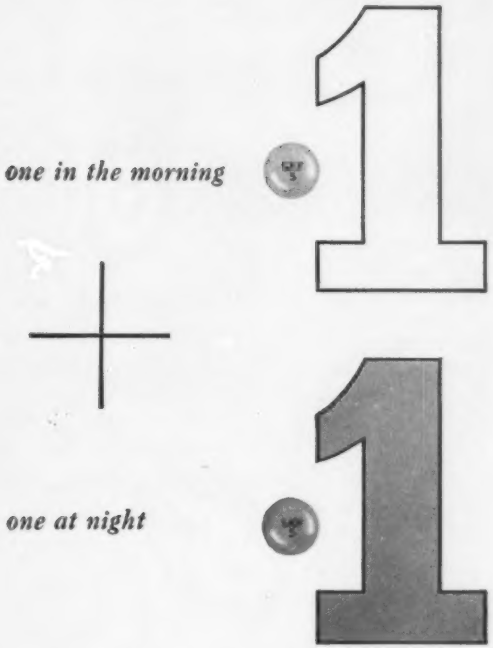
Meprobamate, Wyeth

relieves tension–mental and muscular

Darbid* b.i.d.

"strikingly inhibits basal gastric secretion...

for at least 12 hours"[1]



provides

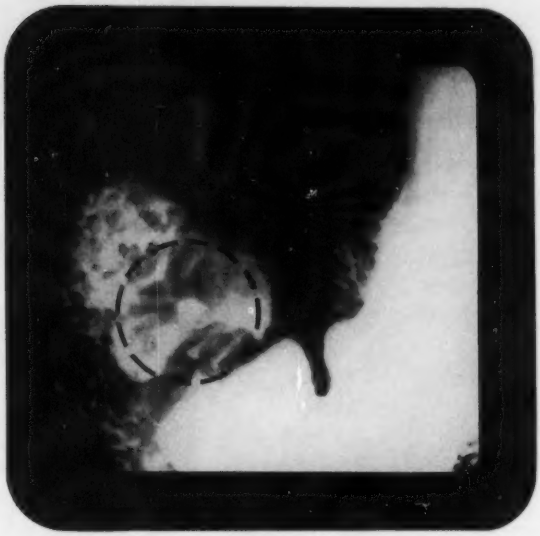
24-hour antisecretory and antispasmodic protection for patients with ulcer and other g.i. disorders

Smith Kline & French Laboratories, Philadelphia

1. Mullie, A.: The Inhibition of Basal Gastric Secretion and of the Gastric Secretory Response to Histamine by 2,2-Diphenyl-4-diisopropylamino-butyramide Methyliodide ['Darbid'] in Man, Arch. internat. pharmacodyn. *106*:447 (June) 1956.

*Trademark for isopropamide, S.K.F.

in the management of duodenal ulcer



safe, dependable acid control

In the management of duodenal ulcer, Gelusil controls acidity safely—maintaining gastric pH within the normal range (3.5—5). Its demulcent action also helps promote healing of eroded tissue. Gelusil is nonconstipating, yet contains no laxative—a fact of particular importance in ulcer therapy.

To protect the patient against nighttime acid pain, Gelusil-Lac provides the proven antacid action of Gelusil, plus the sustained buffering effect of specially prepared high protein (low fat) milk solids.

GELUSIL®

Two tablets (or two teaspoonfuls of Gelusil Liquid) two hours after meals or whenever symptoms occur

GELUSIL-LAC

At bedtime, one heaping tablespoonful, stirred rapidly into one-half glass of water (provides the equivalent of 4 Gelusil tablets). Supplied in 20-dose bottles of 320 grams.

WARNER-CHILCOTT